*"I would have everie man write what he knowes and no more."*—MONTAIGNE

# BRITISH JOURNAL OF ANAESTHESIA

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## EDITORIAL

ON qualification, the student—we hope he will always remain one, at least in spirit—may be perplexed in deciding to which branch of medicine he should devote his life. Opportunity may force the hand of those who falter, but the student can be attracted during the course, perhaps by an able presentation from the teachers, or by practical experience which has given him confidence in his own ability; this will powerfully draw him further to the subject. Dr. Bryce-Smith, writing in this issue, has touched upon our responsibilities in attracting the undergraduate, and upon our ability to do so the future of the specialty depends in good measure.

Teachers should aim to present knowledge so that it will remain deeply in the student's memory long after qualification, and efforts should be made to assess how much does remain. If only a little is retained it should be the right kind of knowledge. What this is, would give rise to controversy even amongst experts and therefore teaching material should be rigorously sifted and carefully prepared. Some would cover a large field, others would narrow the field and make it more intense. A fundamental duty is to teach the student how to find things out for himself.

Every student can discriminate between good and indifferent teaching, and it may be that careful preparation of the material helps to make the distinction, but this is not all, for the born teacher has a personality that inspires. Those who are not fascinated by teaching and all that it implies, even though they may have distinguished themselves in their own subject, do not make the best teachers, and some of them are among the worst.

An ideal medical school needs men and women not only with a satisfactory knowledge of their own subject but with a flare for teaching, and they ought to be profoundly dissatisfied with the static routine which exists in some quarters today. Those who interview consultants for teaching hospital posts should bear this in mind.

Anaesthesia is a small branch of medicine though its ramifications are large. The shortage of anaesthetists in this country has made us glad of all recruits. If any think they are entering an easy specialty they should be discouraged, for such men will surely gravitate into the ruts of technical skill and not much else, and when they go, radical progress will be possible again. A time will come when there will be more freedom in choosing the right kind of graduate. Of what stuff should he be made, and how can this potentiality be detected and later fashioned into the best channels?

*Brit. J. Anaesth.* (1956), **28**, 244

# THE GROUP PHARMACOLOGY OF ANAESTHETIC AGENTS

## I: THE ABSORPTION—ELIMINATION OF INHALED DRUGS

BY

A. R. HUNTER

*Royal Infirmary, Manchester*

PROBABLY no other drugs lend themselves so well to pharmacological considerations on a group basis as do the inhalation anaesthetics. Before, however, the details of their actions are discussed it is necessary to consider the processes which make it possible for them to produce their effects. First they must be transferred by a process of mechanical mixing from the atmosphere in which they are presented, into the patient's alveolar air. Then they find their way by diffusion at a speed governed by physicochemical considerations across the alveolar membrane into the blood circulating through the pulmonary capillaries. They are carried thence in the first instance mainly to the brain, where they exert their specific action, but ultimately they find their way into all the tissues of the body in greater or lesser quantity. Finally, when the administration of the anaesthetic is stopped, the inhaled drug is eliminated by a reversal of all these processes.

### THE ENTRY INTO THE LUNGS

The first process in the absorption of a volatile anaesthetic into the body is its entry into the lung alveoli. This is essentially a mechanical procedure in which there occurs mixing of a known volume of air in the chest with an atmosphere of known concentration. It is brought about by a reciprocating flow of gases. The variables involved are the tidal air, the dead space air, and the capacity of the chest, and it is a simple matter to calculate how long is required to attain concentrations approximating to equilibrium. The mathematical statement of what happens is a geometric progression, i.e. an algebraic expression of a situation in which there is added to the gas in the lungs at each breath an amount of anaesthetic which is a constant fraction of its predecessor. This fraction is determined essentially by the ratio of the effective ventilation at each breath to the functional residual capacity of the lungs.

Neither the physical constants of the anaesthetic agent nor its concentration appear in the expression and the times required to attain concentrations in the lung of 90, 95, and 99 per cent of equilibrium are, in fact independent of these. In other words, if one excludes consideration of the gas which passes from the lung across the alveolar membrane, the time required for this phase of the induction of anaesthesia can be regarded as constant irrespective of the agent used. It is, for all practical purposes, complete in those with healthy lungs in about two minutes. Where disease interferes with mixing of the entering gases this part of induction may be prolonged to seven minutes but it is never any longer (Comroe et al., 1955). The duration can be sharply reduced by hyperventilation and prolonged by respiratory depression, but because it is so short relative to the duration of the next stage, the administration of carbon dioxide solely for this purpose is barely worth while except when agents irritant to the tracheo-bronchial tree are being given.

### THE ENTRY OF ANAESTHETIC DRUGS INTO THE BLOOD STREAM

The essential factors controlling the entry of anaesthetics into the blood stream, are twofold. First, they must cross the alveolar membrane which from the physicochemical point of view can be regarded as a watery solution of protein. Secondly, they must enter into solution in the blood stream. The factors governing the first process are the partial pressure of the anaesthetic drug in the alveolar gases, and the solubility of its vapour in water, the factors influencing

the second process are its solubility in blood and again the partial pressure of its vapour. The rate of diffusion of gases and vapours in any situation is inversely proportional to the square root of their vapour densities. It can, however, readily be calculated that the amount of variation introduced by this factor into the absorption of anaesthetic agents is small in comparison with the other variables involved and for practical purposes it can largely be neglected.

For the consideration of their absorption across the alveolar membrane, anaesthetic agents have been divided by Harris (1951) into three classes. The first group includes substances like diethyl and divinyl ether which have a high solubility in water and in blood. They pass rapidly across the alveolar membrane. Indeed, they pass into the blood at a rate which is in excess of the speed at which comparable amounts of the vapour are taken in in the inspired air. There is thus a tendency to the development of a deficit between the partial pressure of the ether in the inhaled mixture and that in the alveoli (fig. 1). Further, because the solubility of ether vapour in blood is very high the tension rises slowly (fig. 2). In consequence of these two factors the entry of ether into the blood during the induction of anaesthesia is always very slow. These effects have been amply demonstrated by Haggard (1924) in his classical studies of the rise in the concentration of ether in the arterial blood of the anaesthetized dog. He then found that for two hours or more after beginning the inhalation of an ether-air mixture of fixed strength there was a steadily increasing concentration of the drug in the blood stream. Indeed, Henderson and Haggard (quoted by Robbins, 1935) found that only 50 per cent saturation of the body tissues was attained after this interval.

The second group of anaesthetics is exemplified by nitrous oxide and ethylene. These agents have a moderate solubility in water and moderate solubility in blood. They therefore pass across the alveolar membrane at a slower rate than ether; but their water solubility is such that they can cross in quantity sufficient to ensure early equilibrium between the tension of the anaesthetic in the blood leaving the lungs and its partial pressure in the alveolar air (fig. 3). Further, because the actual amount of anaesthetic taken up by the circulating blood is considerably less than that which finds its way into the lungs at a single breath, there is little tendency to the development of a deficit in the lungs as compared with the concentration in the inspired mixture.

There is experimental support for these views. Thus Gray (1954) in a study of the nitrous oxide content of the blood in patients anaesthetized

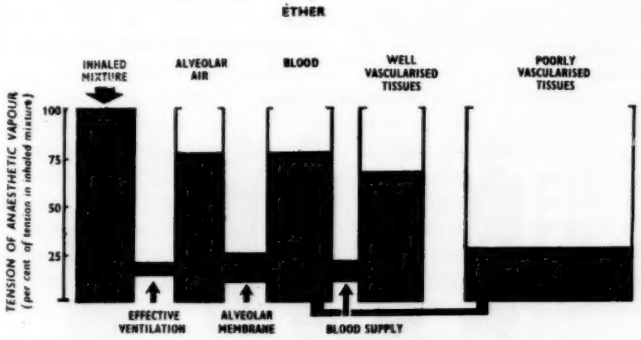


FIG. 1

The absorption and distribution of ether (diagrammatic).
The area of each section indicates the capacity of that structure for the drug, and the shaded portion the amount actually present after the induction of anaesthesia.

Note high solubility in alveolar membrane and blood; lower concentration in alveolar air than in inhaled mixture.

with this agent was able to show that there was little more than five minutes delay in the development of equilibrium between the inhaled gases and their concentration in the blood. These figures contrast sharply with the two hours or more required to attain equilibrium with ether during the experiments of Haggard (1924). The picture for ethylene is not so clear cut, but Nicloux and Yovanovitch (1925) showed that the blood concentration of ethylene in dogs did not increase seriously after twenty minutes' inhalation of the gas (fig. 2).

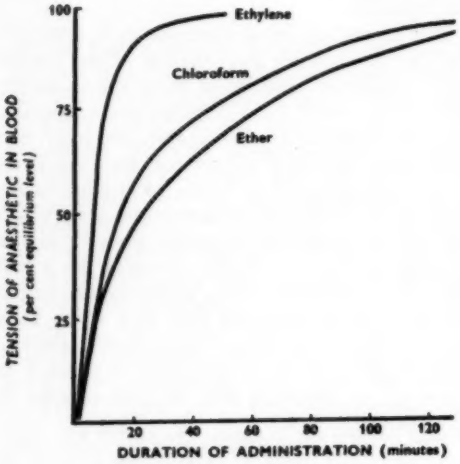


FIG. 2

The uptake of ethylene, chloroform and ether by the blood.
Ether after Haggard (1924); chloroform after Buckmaster and Gardner (1907); ethylene after Nicloux and Yovanovitch (1925).

The last group of inhalation anaesthetics are those which have low water solubility and a low blood solubility. The classic example is chloroform, but the same properties are shared by trichlorethylene, and, to a lesser extent, by cyclopropane. In the case of these agents, the inhaled anaesthetic finds great difficulty in escaping from the alveoli into the blood. The blood tension tends to remain, therefore, considerably below the partial pressure of the drug in the alveoli (fig. 4). There is no rapid loss of inhaled anaesthetic and the alveolar mixture very soon attains equilibrium with the inhaled gases. On the other hand, the barrier opposed by the alveolar membrane to the passage of these agents slows their entry into the blood and equilibrium is attained only a little more quickly than with ether (fig. 2).

Robbins (1935) studied the absorption of anaesthetic drugs on a different basis which neglected the influence of the film of watery solution of protein which comprises the alveolar membrane. He determined the solubility of the agents in blood in vitro, and, expressing this in terms of milligrammes per 100 ml, he related it to the anaesthetic content of the inhaled mixture in the same units. He called this the " distribution ratio ". As would be expected, the findings were somewhat at variance with those of other workers,

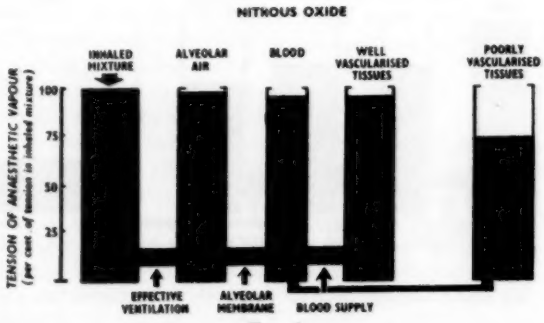


FIG. 3

The absorption and distribution of nitrous oxide.
Note moderate solubility in alveolar membrane, blood and tissues.

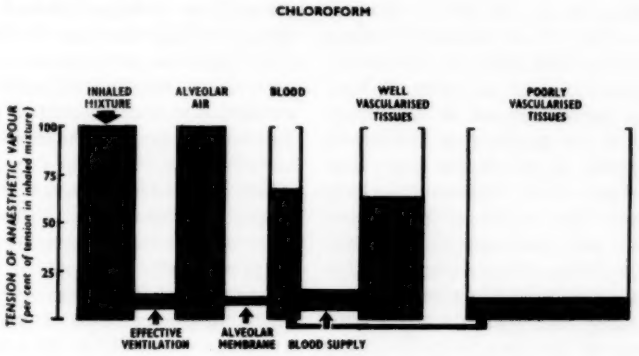


FIG. 4

The absorption and distribution of chloroform.
Note small solubility in blood and alveolar membrane.

but they are none the less interesting to refer to, particularly as the actual concentrations of ether in the blood of animals seem to correspond more closely with those found in clinical anaesthesia than do those of many other workers. On the other hand, the distribution ratio he obtained for ether in vivo was 1:10, while that in vitro was almost 1:14. It is, therefore, apparent that full equilibrium was not attained in the animals to whom he gave this agent. The essential significance of his results with cyclopropane is, however, not quite so clear (Robbins, 1936).

### PRACTICAL APPLICATIONS

These theoretical considerations concerning the absorption of inhaled drugs have a practical application in clinical anaesthesia. Thus during the induction of ether anaesthesia the essential problem is to obtain the entry of large quantities of ether rapidly into the lungs whence it will find its way without difficulty into the blood stream. This can be accomplished, either by hyperventilation with carbon dioxide, or by giving the patient an anaesthetic mixture to inhale containing an amount of ether considerably in excess of that which, at equilibrium, would produce an anaesthetic concentration of the drug in the blood stream. The latter technique has been employed for many years. Its quantitative aspects were studied in neurosurgical cases by Boothby (1914), who, using the Connell "anesthesiometer," gave his patients 13 per cent ether to inhale for the first twenty minutes of the procedure, and then maintained anaesthesia thereafter with something like half this amount; but even this, as Robbins (1935) points out, still represents something like twice the true equilibrium concentration in the inspired air even with a distribution coefficient of 1:10.

Practising anaesthetists have long been aware of a need steadily to reduce the percentage concentration of lipoid soluble anaesthetic agents given to patients as the administration proceeds. indeed this fact was given the title of the "law of diminishing resistance" by Gill (1906). During ether anaesthesia the apparently diminishing resistance of the patient is the result of two factors. First, it indicates the gradual disappearance of the deficit between the tension of the drug in the blood and its partial pressure in the inhaled mixture. Secondly, it reflects the gradually increasing saturation of the tissues with ether, with the result that the administration of the same amount of the drug now produces a much greater rise in blood concentration. It is common knowledge that this law is not applicable to patients under nitrous oxide. This is yet another pointer to the fact that equilibrium between the inhaled gases and the blood is rapidly attained when this agent is used.

The law of diminishing resistance is applicable to anaesthesia with chloroform, trichlor-

ethylene and cyclopropane, but for a different reason. Here the cause of the apparent diminution in resistance to anaesthesia is the slowly rising blood concentration of the drug. Raising the initial alveolar partial pressure of these drugs will tend to hasten the attaining of anaesthetic concentrations in the blood stream; but these high concentrations can relatively quickly became dangerous and overdose phenomena appear. Chloroform and cyclopropane very readily produce respiratory arrest if their administration is pushed. In the case of trichlorethylene, however, the increasing tachypnoea reduces the effective ventilation of the lungs, and the patient is thus preserved from the worst effects of too high a concentration of the drug, though at the cost of some hypoxia.

### THE DISTRIBUTION OF ABSORBED ANAESTHETIC DRUGS

After their absorption into the blood stream anaesthetic drugs are distributed to the tissues of the body. The rate of uptake by any individual structure depends on its blood supply and the solubility of the anaesthetic drug in it. Tissues in which the agent is relatively insoluble achieve equilibrium with the blood concentration fairly quickly, because the uptake of a small amount leads to a large increase in the tension of the drug. Tissues in which the drug is very soluble, with the exception of those with a profuse blood supply, take a long period of exposure to reach equilibrium. For example, the subcutaneous fat, which has a high avidity for anaesthetic drugs and a poor blood supply, seems virtually never to be fully saturated with lipoid soluble agents. Even the brain which has an exceedingly good blood supply requires at least three-quarters of an hour before all the lipoid in its structure becomes virtually saturated.

Apart from some very early studies made about the turn of the century with inaccurate methods, there are comparatively few quantitative investigations of the uptake of anaesthetic drugs by the tissues. There is also a fallacy in this connection which has arisen from an oversimplification. Haggard (1924) stated that the venous blood concentration of an experimental animal exposed to an ether vapour of fixed strength, was a measure of the total amount which the animal had taken up. It was, however, some time before it was appreciated that while this statement is approximately true of the animal as a whole, it took no account of the distribution of the absorbed drugs in the individual tissues of the body.

The details of this aspect of the problem were studied by Dybing and Dybing (1945) in rats. They showed that the brain took up anaesthetic drugs relatively very rapidly; indeed because of the high solubility of ether in the lipoid of the brain, the concentration of this agent, though not its tension, was higher than that in the arterial blood. In the less well vascularized muscles, the rate of uptake was found to be slower, and no doubt the amount of ether in the subcutaneous fat must have been even less.

Direct studies of the uptake of anaesthetic drugs by the tissues were also made by Seevers and his colleagues (1935). They created pockets of air in the subcutaneous tissues and in the peritoneal cavities of experimental animals. They determined the rate at which ethylene and cyclopropane found their way into these pockets, and showed that the passage of cyclopropane inwards was more rapid than was that of ethylene. They ascribe this difference to a slow entry of ethylene into the blood from the lungs, an explanation which is rather surprising in view of the relatively good water solubility and moderate blood solubility of the gas. There are, however, so many factors involved in studies of this kind that it is very difficult fully to reconcile all that is known about the uptake of anaesthetic agents with the various theoretical considerations which seem to govern them. It is, however, interesting that the passage of nitrous oxide into air-containing cavities in the human subject has recently been reported during anaesthesia in tuberculous patients with a pneumothorax or pneumoperitoneum (Hunter, 1955).

### THE ARTERIOVENOUS DIFFERENCE

The reflection of the passage of any substance from the blood into the tissues is an arteriovenous difference in its concentration. Thus the normal individual metabolizing glucose has a higher blood sugar level in his arterial than in

his venous blood. A diabetic patient on the other hand, who is unable to metabolize glucose, shows no such difference. A patient in whom ether is passing from the blood into the tissues shows a similar difference in concentration which diminishes progressively to the point of complete saturation. The capacity of the tissues for absorbing ether is so great that it requires many hours administration before the arteriovenous difference disappears. It is also interesting that the arteriovenous difference in the vessels supplying the brain becomes smaller more rapidly than does the corresponding difference in ether concentration in the mixed venous blood. This once again reflects the more rapid uptake of anaesthetics by the brain because of its better blood supply.

The arteriovenous difference in concentration has also been worked out in some detail by Robbins (1936) for cyclopropane, and he has found that with this agent it is gone after thirty-five to forty-five minutes administration to experimental animals. Presumably the interpretation of this rapid absorption lies in the relatively smaller solubility of cyclopropane in the tissues than that of ether.

### RECOVERY FROM ANAESTHESIA

The laws governing the elimination of anaesthetic agents after their administration are exactly similar to those governing their uptake. The only part of this process which is of interest is the elimination of the anaesthetic substances from the tissues. For within the first few minutes after the withdrawal of any agent its blood concentration and its concentration in the pulmonary alveoli fall to relatively low levels. The elimination of anaesthetic drugs from the tissues is a much slower matter. It has been studied in detail for chloroform by Buckmaster and Gardner (1907), by Haggard for ether (1924), by Robbins (1935) for cyclopropane. With all these agents the process is, as would be expected, exponential in its rate, occurring more rapidly to begin with and tailing off subsequently. The essential problem is the elimination of the drug which has reached the tissues, and once again the governing factors are the solubility of the drug in the blood stream and the effectiveness of the blood supply to the various organs. There is one important difference between absorption and elimination. During absorption the drug finds its way to the brain more quickly than it does to other organs, and the onset of unconsciousness is relatively rapid. During recovery, on the other hand, the tension of the anaesthetic in the brain must of necessity remain always just a little higher than the concentration of the general venous blood (fig. 5). Therefore, as long as the less vascular tissues are pouring anaesthetic into the blood stream, it is impossible for a complete recovery of the central

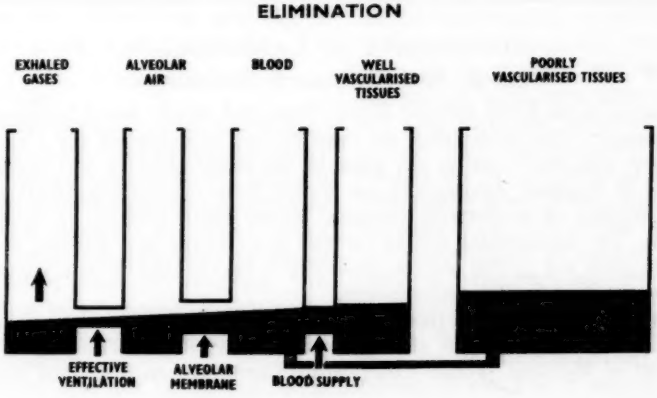


FIG. 5
The elimination of anaesthetic drugs.

nervous system to occur, even though its blood supply is such that, were it isolated from the rest of the body, all the anaesthetic could be removed from it in a comparatively short time.

Because a high partial pressure of nitrous oxide is required to produce anaesthesia, and because its solubility in the tissues is low, this agent is much more rapidly and completely eliminated on stopping its administration. There is, therefore, not the same tendency to prolongation of the recovery period with this agent. Its rapid elimination has, however, one disadvantage, Fink and others (1954) have shown that as much as twenty-five litres of the gas may be eliminated from the body in the first ten minutes of the recovery period. By its bulk this may displace oxygen from the alveoli and give rise to temporary hypoxia which they think might be severe enough to precipitate the collapse of a critically ill patient.

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## EDITORIAL ANNOUNCEMENT

It is recognized that the subscription of £3 15*s*. per annum for the *British Journal of Anaesthesia* might be a heavy burden for anaesthetists in trainee positions, despite the fact that for this subscription they receive twelve monthly issues, including two of special educational interest. Because of our desire to interest aspirants to the specialty in this publication, the publishers have agreed to supply the Journal to *bona fide* trainees in Great Britain, on application for three years at the reduced rate of £2 10*s*. Forms of application for this concession may be had on request to the Editors.

## UNIVERSITY OF CAMBRIDGE

### Elmore Medical Research Studentships

The Managers of the Frank Edward Elmore Fund will shortly award Studentships for medical research. The Studentships are open to male graduates of any University in any country, who were born at any place in the British Empire or Commonwealth other than in Scotland. Applications are invited from medically qualified graduates who are desirous of undertaking research, among other subjects, on problems of anaesthesia. The appointment will be for two years in the first instance at a salary of between £850 and £1,000 per year according to the candidate's experience, whether married or single, and other circumstances.

Applications accompanied by three testimonials, a statement of previous appointments and copies of published papers should be sent to the Regius Professor of Physics, Department of Medicine, Tennis Court Road, Cambridge, to reach him before July 15, 1956.

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# PRACTICAL APPLICATIONS OF ELECTRONICS IN ANAESTHESIA*

BY

G. A. HAY

*Department of Medical Physics, University of Leeds*

## PART II: APPLICATIONS

IN Part I of this article were discussed some of the basic principles of electronics. In particular it was shown how the thermionic triode valve may be used either as a power amplifier or as a voltage amplifier, and how its behaviour in these two circuits may be stabilized. The use of valves in the production and shaping of voltage and current waveforms was also described, and the cathode ray tube was discussed as a means of displaying and recording electrical waveforms. The above circuits and components all deal directly with electrical quantities, but it was further shown how with the aid of transducers these functions could be made available for other variable quantities such as temperature, pressure, etc.

In the following discussion the way in which these principles may be applied to various clinical problems in the field of anaesthesia will be explained, although emphasis will still be laid upon basic principles, so that these ideas may be extended to the solution of other problems.

*Electrical quantities.*

It is well known that the normal physiological functions of nerves and muscles, and indeed of the brain itself, are accompanied by electrical phenomena. It is therefore possible, in principle at least, to attach electrodes to suitable points on or in the organ concerned and to obtain valuable information about its condition. For example, the state of the heart during surgery may be followed by means of a continuous electrocardiographic recording.

The heart muscle was one of the first to be investigated electrically, because it produces currents in the trunk which are large enough to actuate a relatively insensitive detector such as the string galvanometer. This instrument, however, is comparatively fragile and inflexible, and where convenience and portability are required, for example in the operating theatre, valve amplifiers must be used. In other tissues such as muscles and the brain, the voltages and currents produced are very small and there is no alternative to the use of the thermionic valve. We shall therefore consider some special problems encountered in the design of all electrophysiological amplifiers, before considering separate techniques in some detail.

In figure 6(a) is shown a mass of tissue with so-called " monopolar " electrodes in position. The shaded portion represents the source of electrical activity, and electrodes A and E are connected to the grid and filament respectively of an amplifier such as that in figure 3(b) (Part I). The voltage input to the amplifier will therefore consist of the wanted signal upon which are superimposed any other potential differences existing in this region. The commonest of these interference voltages are 50 c/s potentials which are induced from nearby power wiring, and potentials due to the heart itself. The former may at some cost and inconvenience be reduced by screening the patient in a wire mesh cage, but this will not affect the latter.

Still using the same amplifier circuit, a great reduction in interference may be achieved by moving the electrode E very close to A, thus ensuring that the amount of tissue between the electrodes which does not contribute to the signal

*Continued from *Brit. J. Anaesth.*, **27**, 627.

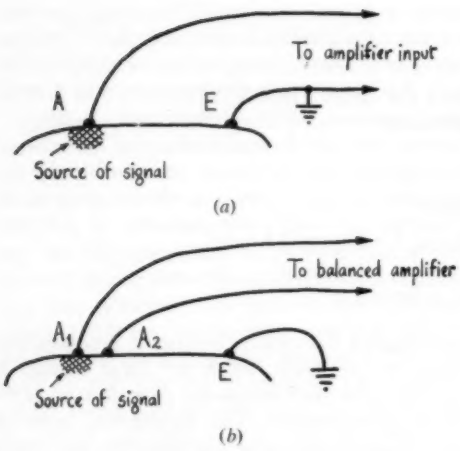


FIG. 6
(*a*) "Monopolar" electrodes used with simple amplifier.
(*b*) "Bipolar" electrodes used with difference amplifier.

is a minimum. In some work this is a very satisfactory expedient; in electromyography, for example, electrodes are used consisting of a hypodermic needle through which has been inserted an insulated wire, the end being ground flush with the needle. The latter is earthed and therefore the central electrode is completely screened. When this electrode system is inserted into the body of a muscle it is sensitive to action potentials arising only very close to the needle tip.

This method, however, is unsatisfactory when two or more pairs of electrodes are used in conjunction with a number of separate amplifiers, as in the case of the "multilead" electrocardiograph or the electro-encephalograph. This is because a number of amplifier channels operating from the same or even related power supplies must have a common earth connection, and therefore a number of different points on the body will be connected to the same earth point. This invariably leads to interaction between the channels, and it will be impossible to be certain that the voltage waveform recorded in any one channel originated exclusively in the volume of tissue between the corresponding pair of electrodes.

For this reason, it is customary in most physiological amplifiers, even those designed only for single channel operation, to use two so-called "bipolar" electrodes neither of which is connected to earth. The arrangement is shown in figure 6(b), from which it is clear that the earthed electrode is included merely for convenience and is independent of $A_1$ and $A_2$. In fact in many situations the apparatus will operate equally well without an earth connection. The electrodes $A_1$ and $A_2$, however, must be connected to a balanced or differential amplifier, in which both input terminals are dissociated from earth. Such an amplifier responds only to the difference between the potentials at $A_1$ and $A_2$ and not to voltages arising between either $A_1$ or $A_2$ and earth. In a practical example the potential difference $A_1$ to E might be composed of an action potential of 100 microvolts and 50 c/s interference of 10 millivolts, and $A_2$ to E might consist only of 10 millivolts of interference. We therefore require an amplifier which will give appreciable gain for the 100 microvolts of signal but give zero output from the 50 c/s interference.

Figure 7(a) shows a simple differential amplifier with the two electrodes connected to the two grids and the output taken from the two anodes. It is clear that if the two valves have linear characteristics and are identical in gain, the output voltage taken between the two anodes will be an amplified replica of the wanted action potential but will not contain any 50 c/s interference component. This is true only if the valves are identical *and remain*

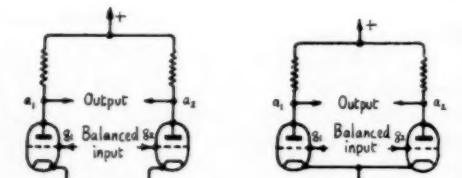


FIG. 7
(*a*) Simple difference amplifier.
(*b*) Balanced difference amplifier with common feedback.

*so* to very close limits of accuracy. In practice this sort of performance cannot be obtained for even short periods; ageing of valves and variations in component values and supply voltages rapidly cause unbalance of the circuit. Fortunately we are able to stabilize the performance of the circuit by means of negative feedback in a manner similar to that shown in figure 3(a). The resulting circuit, which is shown in figure 7(b), is called a " long-tailed pair ", and is a very stable circuit in that it neither disturbs other circuits by interaction through common power supplies nor is it disturbed by them. The cathode resistance has the effect of reducing the gain of the stage to less than unity for interfering voltages without affecting the differential gain, which is usually of the order of 10.

The output of such a stage needs further amplification, and in a complete physiological amplifier it is usual to have a number of long-tailed pairs in cascade so that the output of one forms the input of the next. In this way voltage gains of the order of several million are possible with reasonable stability, thus an input of, say, 100 microvolts will become 100 volts at the output. This is sufficient to give adequate deflection of the beam of a cathode-ray tube and thus to present the output in visual form on the screen. At first sight it may appear that there is no limit to the voltage amplification which may be obtained from a sufficient number of valve stages. In practice, however, the maximum usable gain is limited by considerations of stability and, more important, by the " granular " nature of the electric current. Thermal agitation of free electrons in conductors together with the " hailstorm " effect of the electrons forming the anode current in a valve produce a background of electrical noise which is equivalent to a random signal of about 2 to 10 microvolts at the input terminals of the amplifier. The noise arising in the first stage is amplified most, and therefore great care must be taken with its design. For this reason and also because it is largely responsible for discriminating against interference the input stage of a physiological amplifier —and indeed of most other electronic devices— can determine to a large extent the standard of performance of the whole equipment.

Another point which is of general importance arises from this idea of noise level. So that the required signal may be readily distinguished above the noise it is most important to ensure that the connection between the living tissue and the amplifier provides the most efficient possible transfer of signal. Only then will the " signal-to-noise ratio " be a maximum. On the other hand, if the noise arises in the biological material it will be inseparable from the signal by any external means. This general principle is applicable to most electronic systems and is readily demonstrated with an ordinary radio receiver by using only a few inches of wire for the aerial. The signals will then be audible only against a strong background of noise which is generated within the set itself. The design of electrode systems for use with electrophysiological amplifiers is thus an important consideration, although in some cases the efficiency of the electrodes is necessarily severely limited by human anatomy.

We may now consider some specific techniques in greater detail. The electrical activity of the heart provides a valuable guide to its condition, and quite apart from routine electrocardiographic examinations it is becoming customary to record the heart's activity, if not continuously, at least at regular intervals throughout the duration of a surgical operation. The necessity of working electronic apparatus in the operating theatre itself raises new problems. The equipment must be easily portable and must not interfere in any way with theatre routine. It must be robust, easily cleaned, and incapable of igniting explosive mixtures of gases. These requirements are reasonably easy to satisfy, and several commercial mains-operated instruments are available. They all conform to the general pattern of physiological amplifier previously described, except that for reasons of convenience a cathode-ray tube is not used for displaying the output.

There are three main types of recorder available as alternatives to the cathode-ray tube. They all contain an electromagnetic driving unit similar to a moving coil meter, but designed with as low inertia as possible so as to follow rapid changes in output voltage or current. The fastest of these has mounted on the moving element a small mirror which reflects a light beam on to a moving strip of photographic paper. These recorders will

follow a voltage change in a time as short as 200 microseconds, but their record needs photographic development and is therefore not immediately available for inspection. A second most ingenious design uses a very fine jet of special ink which writes directly on a strip of paper, the record being blotted by passing over an absorbent roller. This pattern is capable of following a 500 microsecond change, and its record can be inspected as soon as made. The third method consists of the same type of driving unit but with a light stylus which moves over the paper strip and makes a mark in a variety of ways, either by ink feed through a hollow stylus, by an electrical discharge, or by a heated writing point. Whatever the method of marking, the record is instantaneous and permanent, but the inertia of the stylus limits the speed of this type of recorder to about 3 milliseconds. This, however, is adequate for routine electrocardiography. It is usual in all types of recorder to make provision for a variable paper speed and in some cases for time marking. For long periods of recording it is most economical to use a slow paper speed, but this results in a compression of the waveform, which may give rise to difficulties in reading.

A more serious problem in the operating theatre is caused by the handling to which the patient is subjected and by interference from other electrical equipment which may be in use at the same time. These difficulties are not acute in electrocardiography, but it is generally necessary to earth the patient with a saline pad of large area and to return all other earth connections to it. This electrode can conveniently be the "earthy" pad of a diathermy apparatus, and then it should be possible to leave the diathermy connected to the mains but switched off. It is generally impracticable to take any records while the diathermy equipment is in use. Normal handling, including the use of surgical instruments, should not interfere with a record if the e.c.g. electrodes are placed well away from the area concerned. The surgeon, in his preoccupation with his own complex task, is apt to be rather intolerant of masses of electrical apparatus which have no immediately obvious application, and his co-operation must be obtained beforehand, preferably by convincing him of the clinical value of the measurements being made.

The electrical activity of the brain is being used to an increasing extent as an index of depth of anaesthesia. In routine electro-encephalography it is usual to have six to eight separate amplifier channels associated with a number of pairs of electrodes suitably disposed about the head. In such a technique, to avoid interaction between channels, it is essential to use balanced amplifiers in which neither input terminal is earthed. The amplifiers are conventional but have a rather higher gain than usual because the voltage waveforms derived from the scalp are of the order of 20 to 50 microvolts only. The brain potentials measured on the cortex are about 50 to 100 millivolts in amplitude, but they are attenuated by a factor of a thousand or so in their passage through the skull. For this reason it is imperative that the noise level of the amplifier should be very low, and the technique affords an excellent example of the serious effects resulting from an inability to make best use of the original signal. In most cases it is impracticable to make direct connection to the cortex.

For use in the practice of anaesthesia it is unnecessary to have more than one channel of amplification, and it is often convenient to make use of an existing direct writing electrocardiograph, the recorder of which will have ample speed for e.e.g. work. It is necessary, however, to add another valve stage in the form of a pre-amplifier, which may be a longtailed pair giving a gain of about ten. Because of the limited signal available and the extra gain which is necessary, it is found that such an arrangement in the theatre is extremely susceptible to interference from mechanical movement of the patient and from other disturbing factors. This difficulty may be greatly minimized by the use of an electrical filter network which selects a band of frequencies and partially suppresses those which lie outside this band. To clarify this point we must consider in more detail the significance of the shape of the waveform being examined.

If an electrical quantity such as current or voltage is continuously changing, the way in which it varies with time, as depicted graphically, is called its waveform. An important principle, enunciated by Fourier, states that any periodic waveform may be resolved into a number of sinu-

soidal components of different frequencies, or conversely that the synthesis of these components will produce the original waveform. Thus, although the e.e.g. recorded from one pair of electrodes must necessarily be a single waveform of complex shape, it may be analysed into a number of components which range from 3 to 40 cycles per second. For this reason we speak of the output of a single channel as containing these separate components although there is present only a single varying voltage. In using the e.e.g. as an index of depth of anaesthesia, we are not so much concerned with the waveform itself as with the relative amplitude of the activity within a frequency band of, say, 3 to 14 c/s. As handling of the patient will usually produce interference components of frequency less than 3 c/s, it is clear that a simple filter which accepts the above mentioned band will to a certain extent reject the electrical manifestations of mechanical movement. At the same time it will also reject 50 c/s interference originating in the supply mains. The output waveform of the filter will be different from the input, but their amplitudes will be proportional. Electrical filters are normally composed of capacitances and inductances in the form of condensers and coils, but when the filter characteristics are not critical, as in the present example, a simpler design results from the use of capacitances and resistances.

With the e.e.g. record available as a guide, the anaesthetist can then regulate the administration of the anaesthetic as experience dictates. Certain workers have carried the technique farther and have allowed the output from the e.e.g. amplifier to control the anaesthetic directly without human intervention. This requires additional circuits in which valves are used as control elements, and the implications of the system will be discussed later under that heading.

*Non-electrical quantities.*

In Part I the transducer was mentioned as a device for converting one form of energy into another, and our particular interest now is in those systems in which one of the energy forms is electrical. For example, a thermocouple may be used to give an electrical indication of temperature difference or a pressure transducer to produce continuous recordings of blood pressure. The correct operation of the whole system depends upon the manner in which the transducer converts, for example, pressure changes into voltage changes, and therefore its design is often critical and difficult. We shall discuss the measurement of intravascular blood pressure in some detail as it affords an excellent example of the conflicting requirements which may be met in practice.

In the direct measurement of blood pressure a needle or catheter is inserted into a blood vessel, the other end communicating with the transducer. Piezo-electric crystals, strain gauges, and other devices have been used in pressure transducers, but there are many capacitance-type gauges in use, and our discussion will be limited to these. Figure 8 shows in cross-section the essentials of a capacitance manometer. A volume of saline communicating with the blood stream via a needle or catheter is bounded on its upper side by a stiff metal diaphragm, the latter, together with the body of the instrument, being earthed electrically.

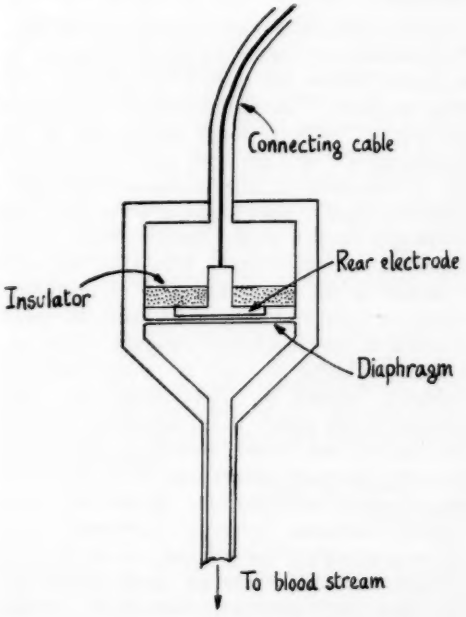


FIG. 8
Diagram of a typical capacitance manometer.

At the other side of the diaphragm and spaced from it by a few thousandths of an inch is a rigid electrode insulated from earth and forming with the diaphragm a condenser of small capacitance. The rear electrode is connected via a coaxial cable to an electronic unit which converts changes of capacitance into voltage changes, and the latter are then fed to a power amplifier and pen recorder.

If the pressure in the liquid is atmospheric the diaphragm will be in its undeformed state, and the recorder is then manually adjusted to read zero. From this position an increase or decrease of pressure will produce a corresponding change in capacitance which will be converted into a change in voltage output and thus recorded. The transducer and its associated circuits may thus be calibrated in terms of pressure. The principal requirements in its design are then: (1) linearity between pressure and capacitance change; (2) stability of zero; (3) sensitivity consistent with small volume displacement; and (4) speed of operation.

In some ways these requirements are conflicting. The problems are mainly mechanical, however, as electronic circuits can easily be designed to fulfil these conditions. The relation between capacitance and pressure is linear for a deformation of the diaphragm of 1 or 2 per cent, and the sensitivity may be increased by using a thinner diaphragm. There is a limit to this process, however, as a thin diaphragm exerts a smaller restoring force on the oscillating column of liquid. This will result in a reduction in the maximum speed of operation, which for linearity must not approach the speed at which the system oscillates naturally. Moreover, a thin diaphragm is much more susceptible to deflection beyond its elastic limit, and zero instability may result. If the apparatus is to be convenient in use, the zero stability should be such that only infrequent checks need to be made during a series of measurements. At least one commercial manometer, however, is extremely sensitive to temperature changes, and it is necessary to perform zero and calibration checks before and after each single pressure measurement. Sensitivity to thermal gradients is a function of mechanical design, and it is extremely difficult to produce an instrument which will be entirely free from these troubles.

Subject to these exceptions, it is not difficult to make satisfactory recordings of intravascular blood pressure to an accuracy of 5 to 10 per cent in the operating theatre, but care is necessary in using the apparatus. In many investigations, however, it is sufficient to have a record of the systolic and diastolic pressures as indicated by a sphygmomanometer, and this may be done by an electronic system which replaces the human operator. The normal process of measurement is well known; a cuff designed to occlude a main blood vessel by the application of a measured pressure is alternately inflated and deflated until the pulse as detected by a stethoscope respectively disappears and appears. There are four processes involved in the measurement: (1) detection of the pulse sounds; (2) interpretation of the sounds; (3) control of the pressure in the cuff; and (4) recording of the pressure. All these functions may be performed electronically, and the method then forms a good example of a common electronic system known as a servo system, which we shall discuss in some detail in the next section.

*Control by electronics.*

In a sense all electronic circuits may be said to embody an element of control: for example, the so-called amplification produced by a triode is effected by the control of the local anode current by the signal voltage. In a more limited sense, however, we may use triodes (and other valves) either to control mechanical functions or to replace mechanical control devices. For example, in the traditional X-ray generator the main high-tension current is switched on and off by electromagnetic relays which must necessarily handle large currents and are therefore large, slow, and liable to contact burning and short life. In some recent designs these relays have been replaced by triode valves which act as thermionic relays, the anode current being switched on and off by making the grid respectively positive and negative. This type of control has all the advantages of the thermionic device such as speed, silence, absence of moving parts and reliability.

Alternatively the valve may be used as an intermediary between a signal voltage, derived per-

haps from some body function, and a mechanical device. For example, in the automatic sphygmomanometer mentioned above the inflation of the cuff is regulated by pneumatic valves which are in turn controlled by thermionic valves. The input to the thermionic valves consists of the output, suitably amplified and shaped, of a microphone which is arranged to detect the pulse sounds. Pressure is allowed to increase in the cuff until the microphone ceases to register any sounds, when the rise of pressure is halted and its value recorded. The pressure is then released and after a suitable interval the process is repeated. The method possesses all the elements of a negative feed-back system as described in Part I; in fact a servo system always consists of a negative feed-back link which usually contains mechanical components.

Such a system may also be used to control the administration of an anaesthetic in terms of the output from a single channel e.e.g. as mentioned previously. It must be very clearly realized, however, that a servo system which does not include the human brain is extremely limited in its scope, in that it will deal in a stereotyped way only with the single set of conditions for which it was designed. It cannot deal with any emergency which may lie outside the range of those conditions. It seems, therefore, that to deprive such a system of the complex and varied experience of the human brain is a step which should be taken only when such a course is unavoidable or when the consequences of failure in the system would be relatively trivial. For this reason it seems desirable to retain the human element where the giving of an anaesthetic is involved.

A further example of electronics used in control seems at first to invalidate this argument. In recent years apparatus has been designed to simulate the action of heart and lungs for short periods. To control the speed of action of such devices, transducers operating in conjunction with valves and responding to such variables as blood pressure and blood flow are used. In this case it would appear that the inclusion of the human link would be desirable to take care of emergencies. The "sensory" indications, however, are much more precisely defined and reliable than the electro-encephalogram and, moreover, the rate of arrival of information is higher than could conveniently be handled by human agency. In this case it is necessary and indeed reasonable to take advantage of the speed of the electronic system.

In this short summary no attempt has been made to discuss in great detail or to give references to specific methods. These may be found in the literature, in most cases together with full descriptions of apparatus and procedures. Rather have we tried to show the basic functions which electronic systems are capable of performing, and it is hoped that in this way a better understanding may be gained of the many techniques now available to the clinician.

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## CORRESPONDENCE

### BARBITURATES FOR OBSTETRICS

Sir,—Although Dr. Collier (p. 130) has adequately stressed the potential dangers from the injudicious use of barbiturates for Caesarean section, attention should be drawn to more recent publications on their placental transmission. Contrary to the findings of Hellman et al. (1943), which he quoted, McKechnie and Converse (1955) found that the maximum concentration of thiopentone in mixed cord blood was reached within about three minutes after its administration to the mother. Kahn, Nicholson and Assali (1953) using thiamylal found that equilibrium was reached between the maternal and foetal blood within four to five minutes of its injection and that the equilibrium was maintained over a period of at least one hour.

On reading Dr. Collier's paper, one might get the impression that a large dose of thiobarbiturate could be safely given for a forceps delivery, if the procedure was expected to be complete within five minutes, whereas more recent work has shown this to be untrue.

JOHN W. DUNDEE
(*Philadelphia*)

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# TETANUS AND THE ANAESTHETIST

*A Review of the Symptomatology and the Recent Advances in Treatment*

BY

J. J. L. ABLETT

*General Infirmary, Leeds*

## INTRODUCTION

TREATMENT of this preventable disease is purely symptomatic and is a carefully integrated attack aimed at supporting life until the disease process has worn itself out. With advancing knowledge of physiological and pathological processes, this has become a most complex problem requiring much diversion of human effort. While this may be possible in the larger centres where experienced staff and full auxiliary services are available, it so happens that in the more highly civilized communities tetanus now is rare and experience of the disease itself hard to gain. On the other hand, in those countries where the disease is common, adequate facilities, both staff and equipment, are so often lacking. A form of treatment possible in one centre may be quite inapplicable in another, and even in the most fully equipped hospital, the best therapeutic regime has yet to be devised.

These facts must be remembered when assessing newer methods of treatment and comparing mortality rates, a rate which in this country remains disconcertingly high.

The anaesthetist, because of his specialized knowledge of respiratory physiology and its application to the paralyzed or unconscious patient, is now frequently an active member of the therapeutic team. The purpose of this paper is to present a brief review of the disease, and to discuss some of the problems of symptomatology and treatment in severely ill patients.

## INCIDENCE AND MORTALITY

Tetanus is not notifiable in England and Wales. Its general incidence, estimated at approximately 150 to 200 cases a year, can only be inferred from the mortality statistics of the Registrar-General, and from the average case mortality of published series. Two recent reports quote a mortality of 42 per cent at Aberdeen (Galloway and Wilson, 1955), and of 30 per cent at Oxford (Honey et al., 1954). Figures may well be higher at smaller hospitals, where an admission might be a rare event.

The average yearly number of deaths have been: for the decade 1934–43, 102 (variation from 126 to 85); for the decade 1944–53, 73 (variation from 88 to 61); in the year 1954, 37; a significant fall.

The mortality (and by inference, the incidence) is highest in childhood, lowest in the middle years of life, and rises again after the age of 50. Active immunization of Service personnel is probably directly responsible for the lower incidence in the middle years (Coneybeare and Logan, 1951).

## PATHOGENESIS

Clostridium tetani produces spores which occur naturally in soil and in the intestines and excreta of animals. They are highly resistant and can remain dormant for years.

Germination is anaerobic and in wounds depends on the oxidation-reduction potential of the tissues (Wright, 1954). If this is reduced, the spores can develop; if not they remain in the tissues, some to be destroyed by phagocytes; but some may continue latent and capable of germination later, for instance after a re-exploration of the wound. During development they produce a neurotoxin which is absorbed into the blood stream (the "circulating" toxin), and which eventually reaches the nervous system (the "fixed" toxin), where it probably affects the anterior horn cells in the spinal cord, and the cranial nerve nuclei and basal ganglia in the brain.

Two forms of tetanus appear to exist, both experimentally and clinically: "local" tetanus and the classical "general" form, the type usually seen in man. This has led to much controversy regarding the route taken by the toxin, but the bulk of evidence suggests a centripetal spread up the regional motor nerves from the motor nerve endings to the spinal cord and brain stem (Wright, 1954, 1955), though some maintain that it is blood borne direct to the affected cells (Abel et al., 1935).

The mode of action and the nature of injury inflicted on the cells are not known (Wright, 1955), though Brooks et al. (1955) have reaffirmed its similarity of action to strychnine.

The effect, unlike that of strychnine, is a progressive tonic spasticity of all voluntary muscles, protagonists and antagonists alike, and superimposed on this, reflex convulsions may occur. Aberrant forms are known in which paralysis, not rigidity, is the predominant feature, as occasionally seen in "cephalic" tetanus (Bagratuni, 1952).

Baker (1942, 1943), when studying the histopathological appearances, found that the cranial nerve nuclei were more extensively poisoned than the anterior horn cells; there was often a selective involvement of these nuclei, notably of the 5th and 10th. Occasionally, there appeared to be a direct involvement of the medulla, accounting possibly for the sudden cardio-respiratory collapse and death occurring sometimes in a patient who appeared to be improving.

These deductions, if correct, are of considerable clinical importance, for most of the changes described by Baker (1942) were reversible. The balance may well be tipped unfavourably if, to this toxaemia, the effects of anoxia and depressant drug therapy are added.

## SYMPTOMS AND SIGNS

1. *Tonic rigidity.*

The commonest early symptom is trismus, associated frequently with a difficulty in eating and swallowing, and a stiffness and aching in the neck and back. Gradually, as the muscles tighten up so the body becomes stiff and extended. The face shows the typical risus sardonicus, furrowed forehead and clenched jaws. The neck is stiff, with resisted flexion, the erector spinae muscles in tonic contraction, and later there is marked opisthotonus. The abdomen is board-like, but not tender, the thoracic cage rigid and deep inspiration is restricted. The limbs are the last, and the least, to be affected, while the reflexes are normal, or increased.

The state of generalized tonic rigidity persists throughout the illness until recovery or death. In mild cases it may progress no further, but usually it gradually increases in intensity, and it may be many days before it reaches a peak. Concurrently, there is an increase in reflex excitability, the slightest stimulation or manipulation evoking an exaggerated response, with painful cramp-like muscle contraction. This state waxes and wanes unpredictably and is itself a prelude to the reflex spasms or convulsions to follow.

2. *The reflex spasms (convulsions).*

These are by far the most frightening and dangerous feature of the disease. They are characterized by a violent rigidity, usually sudden in onset, but sometimes working up to a crescendo, with every single voluntary muscle in the body thrown into intense, painful tonic contraction. The eyes stare, the jaw clenches, the tongue is bitten, the neck is retracted, the back arched, and opisthotonus is extreme. Often there is a muffled inspiratory cry, as the diaphragm contracts and draws air through the apposed vocal cords. Finally, laryngeal spasm becomes complete, the chest fixed and respiration ceases from muscle spasm. At the same time there is a gross outpouring of secretion, with profuse perspiration and foaming at the mouth.

Such an attack varies from a fleeting stiffening of a few seconds, with a slight increase in pulse rate and little effect on respiration, to the severe convulsion with a rapid bounding pulse and cessation of respiration, perhaps with cyanosis. The attack may last several minutes, and as it passes off, the patient lies exhausted, but he can never relax. Such spasms are quite unpredictable, both as regards their violence and their frequency, but the more severe the disease, the more frequent and severe are the convulsions.

They may be provoked by (*a*) external stimuli, such as noise, movement, and light; (*b*) internal stimuli, such as attempts to swallow, to talk, or

to cough; by abdominal colic or the desire to micturate; or (c) " spontaneously ".

*Death* may be rapid from direct asphyxia; or, later, from exhaustion and cardiac failure; from central medullary failure, either from the direct action of the toxin, or from anoxia; from respiratory infection; or from the treatment itself, when so often the immediate cause is in doubt (Saint, 1953).

## CLINICAL TYPES

Six clinical types are recognized (Knott and Cole, 1952) which, however, merge into each other.

*Type* 1. Local, usually mild and confined to the region of the wound, though it may take one of three forms (Millard, 1954).

(a) Purely local.

(*b*) Local, later becoming general.

(*c*) General, becoming secondarily local.

*Type* 2. Generalized tonic rigidity, which gradually increases and then slowly passes off without spasm, the whole process lasting 1 to 4 weeks.

*Type* 3. Generalized tonic rigidity, passing into reflex spasms and gradually becoming more severe. They may then subside, with recovery, or get worse until death.

*Type* 4. In which the muscles of deglutition and respiration are mainly affected, with less emphasis on generalized spasm; said to be usually fatal.

*Type* 5. Cephalic tetanus, a form of local tetanus in which actual paralysis of a cranial nerve is the usual feature; this carries a good prognosis.

*Type* 6. Tetanus neonatorum, from infection of the umbilical cord; this carries a high mortality.

## PROGNOSTIC CRITERIA

The severity of the disease is proportional to the rapidity of its onset. Two factors help to determine the likely severity.

(1) *The incubation period* is the time between injury (when known) and the first symptom. Under 7 days, the prognosis is bad; between 7 and 14 days, it is equivocal; over 14 days, the chances are good. In many patients, there is no wound (Cooke, 1948, found none in 20 out of 57 tetanic children).

(2) *The period of onset* is a more accurate indication of the severity and is the time between the first symptom and the first generalized reflex spasm. Under 48 hours, the prognosis is bad; over 7 days, reflex spasms are unlikely to develop. The chances increase with every day that convulsions are delayed.

Other factors to be considered are:

*Of unfavourable significance.*

(1) A severe or septic wound.

(2) The extremes of age—infancy or over 60 years.

(3) Pre-existing disease (especially pulmonary.)

*Of favourable significance.*

(1) Previous active or passive immunization.

(2) The presence of local tetanus.

(3) A healthy patient.

By a careful consideration of all these factors patients can be divided into three prognostic groups (Cole, 1951; Saint et al., 1953).

*Group* 1. Incubation period long, over 14 days; no spasms—a good prognosis.

*Group* 2. Incubation period 7 to 14 days; period of onset over 2 days. Reflex spasms of moderate severity, but may be severe. Prognosis equivocal.

*Group* 3. Incubation period under seven days. Period of onset under 48 hours. A rapid development of severe and frequent spasms. The prognosis is very poor.

These criteria serve only as a guide, as this is a variable disease (Cole, 1935; Godman and Adriani, 1949). In some patients, it is said, no treatment will avail (McIntyre, 1953), since death or survival depends almost entirely on the dose of toxin absorbed before antitoxin is given (Cole, 1953), though some doubt has recently been cast in this fatalistic view (Shackleton, 1954). Reports of patients treated, therefore (and failures are as important as successes), should contain all the details of the treatment and the full prognostic criteria, so that these may be used to assess the newer forms of treatment based on the conventional methods (Cole, 1953; Bodman, 1954).

## IMMUNIZATION

Man has no natural immunity to tetanus. Indeed, an attack does not necessarily confer

protection, for a recurrence of the disease has been reported in at least 55 instances (Martin and McDowell, 1954). These authors report the interesting occurrence of a Negro heroin addict who was readmitted to a New York hospital with the same complaint only 9 months after his discharge, his wife having died a short time before, 3 days after the onset of similar symptoms.

*Passive Immunization.*

This is by injection of antitoxin. The prophylactic dose is 1,500 to 3,000 international units (1950) of antitetanic serum as soon after the injury as possible. Allergic reactions are frequent and the protection is temporary.

*Active Immunization.*

Toxoid is used. Two injections, each of 1 ml, the second given after an interval of 6 weeks, with a " booster " dose 1 year later. Its effect will last many years and its value is beyond doubt. In the last World War there were 35 patients with tetanus in 300,000 British and Commonwealth wounded (Cole et al, 1952), and only 12 in two and three-quarter million admissions to hospital for injuries in the American forces (Stafford et al., 1954).

Active immunization is now advocated: (*a*) for all those exposed to occupational risks of infection; (*b*) in infancy (as in the present field trials with " triple " vaccine); (*c*) in the convalescent stage of clinical tetanus; (*d*) in an injured person, previously actively immunized, when a booster dose of toxoid should be given—not prophylactic antitetanic serum.

## RESPIRATORY PROBLEMS OF THE SYMPTOMATOLOGY

Many recent authors (Herzon et al., 1951; Van Bergen and Buckley, 1952; Woolmer, 1953; and others) have stressed the importance of the airway. Some aspects of this problem will be discussed.

1. *Neuromuscular Dysfunction of Peripheral Origin (Spinal Cord).*

In normal muscle movement voluntary or reflex contraction of a muscle (excitation of the protagonist) is accompanied by simultaneous relaxation (reflex inhibition) of its antagonist (Best and Taylor, 1955).

In tetanus there is generalized tonic spasticity which affects all the muscles of respiration, frequently with simultaneous activity in both protagonists and antagonists. This in time causes:

(*a*) A shallow respiration, with, in severe cases, tachypnoea and progressively smaller tidal volume, as the total minute volume rises from exertion and metabolic needs.

(*b*) A reduction in vital capacity due to restriction of forced inspiration and expiration.

(*c*) Loss of effective cough reflex.

(*d*) In reflex convulsions there may be complete respiratory standstill with all muscles in violent spasm.

2. *Dysfunction of Central Origin (Brain Stem).*

All cranial motor nerves are involved, with often a selective and exaggerated effect on certain nuclei, notably the 5th and 10th (Baker, 1942, 1943); to a lesser extent the 7th, 9th, 11th, and 12th. The resultant dysfunction of the pharyngeal and laryngeal reflexes in particular is of fundamental importance.

Swallowing becomes difficult or impossible. Secretions collect, and, since the patient cannot expectorate, they either pass out through the nose or mouth or overflow on to the larynx.

The normal laryngeal mechanism is disturbed. The voice changes, often to a mere squeak. The adductors being stronger than the abductors, the laryngeal aperture becomes a slit, with resultant stridor and reduced airway. Frank laryngeal spasm occurs on the slightest provocation; locally from above, from the overspill of pharyngeal contents; locally from below, from tracheobronchial secretions and the desire to cough; remotely, from manipulations and movement; generally, as part of a reflex convulsion.

The cough mechanism is disorganized; peripherally, by the spasticity of the respiratory muscles preventing adequate inspiration, and also by the laryngeal dysfunction; centrally, by the direct action of the toxin, and by hypoxia and depressant drugs acting on the medullary centres.

The larynx, therefore, is no longer the protective watchdog of the lungs, and the inhalation of pharyngeal secretions and the stagnation of bronchial secretions become common complications.

Further, as the disease progresses, there may be evidence of central medullary failure, either from the toxin itself, or from the effects of the disturbed airway, intercurrent infection or treatment itself.

3. *Mechanical Obstruction of the Airway.*

Several factors combine to restrict the airway:

(*a*) Trismus, which may be so severe as to prevent any separation of the jaws.

(*b*) Trauma to the tongue, which may become swollen.

(*c*) Salivation and pooling of secretions in the mouth and pharynx.

(*d*) The presence of a nasal tube, blocking one nostril.

(*e*) Laryngeal spasm or oedema.

(*f*) Rigidity of the respiratory muscles.

(*g*) Stagnant secretions in the trachea and bronchi.

(*h*) Pulmonary collapse, infection or oedema.

4. *Alterations in Chemical Physiology.*

As the disease progresses, the tonic spasm of the muscles, the low volume rapid tidal respiration, the restricted airway and the sudden convulsions, combine to produce hypoventilation. The hypoxia with acute anoxic episodes causes increasing restlessness and dyspnoea, which are, in turn, a further stimulus to the tetanus, and a vicious circle starts. At the same time there is retention of carbon dioxide, increased by the excessive metabolism and the violent exertion, and this causes further restlessness and dyspnoea. Respiratory decompensation sets in and acidosis ensues. Eventually the anoxia and hypercapnoea together or separately may cause central medullary depression and failure.

## TREATMENT

As soon as the diagnosis is established arrangements must be made to provide constant supervision of the patient. Vigilance at this early stage is as important as later, for a sudden crisis may arise at any time, especially if the incubation period has been short. If possible, special nurses should be allocated, a quiet darkened room obtained, and suction and resuscitation apparatus provided, with a selection of suitable endotracheal cuffed tubes, laryngoscope, and ampoules of a muscle relaxant.

Treatment and the later arrangements will depend on the initial severity and subsequent progress of the disease, but in ill patients the full resources of the smaller hospital may be considerably strained in order to give the best possible chance of survival.

The anaesthetist, if it is likely that he may be asked to take part, either for emergency resuscitation or in planned treatment, should be notified early so that he may assess the particular problems that concern him, in full consultation with his colleagues.

The general principles of treatment are more conveniently considered under five main headings:

(1) The prevention of further absorption of the toxin.

(2) The protection of the lungs and the prevention of intercurrent infection.

(3) The control of reflex spasms and tonic rigidity.

(4) The maintenance of strength and fluid balance.

(5) General management, including nursing and organization.

### (1) PREVENTION OF FURTHER ABSORPTION OF THE TOXIN

1. *Neutralization of "circulating" toxin.*

Antitoxin must be given as soon as possible. Usually, 100,000 to 200,000 international units (1950) of antitetanic serum are given to neutralize the free "circulating" toxin in the blood stream. It has no action on the "fixed" toxin in the nervous tissue and has no effect on the subsequent development of the disease. Opinion is divided as to whether further doses of antitoxin should be given later. The intravenous route can be dangerous because of the serious, even fatal, anaphylactic collapse that sometimes occurs; intramuscular injection is considered preferable.

2. *Toilet of the wound (if present).*

This is usually of secondary importance. Anaesthesia for such an operation, however minor, should be undertaken with great care because of the ever present danger of laryngeal spasm or reflex convulsion. If further surgical operations are contemplated, for example tracheotomy, it may be

wiser to perform all operative procedures at one anaesthetic session.

### (2) PROTECTION OF THE LUNGS

Most of the respiratory troubles occurring in tetanus are preventable. The most common cause of death—up to 95 per cent—is some respiratory complication, whether from direct asphyxia in severe spasm or other mechanical obstruction; or from the indirect effects of anoxia; or later from the results of secondary infection. At one centre, for instance, 16 out of 17 deaths were directly attributable to pulmonary complications (Honey et al., 1954).

Undue reliance is too often placed on the antibiotics. Valuable as they are in preventing infection, they cannot overcome mechanical obstruction or hypoxia. More active measures are necessary.

Active protection of the lungs involves three main principles:

(1) Maintenance of a clear airway, if necessary by tracheotomy.
(2) The prevention of obstructive pulmonary complications.
(3) The prevention of secondary lung infection.

1. *Maintenance of a Clear Airway.*

In all but the mildest cases the maintenance of a clear airway becomes increasingly more difficult as the disease progresses.

(1) *Oropharyngeal airway.* To overcome trismus and to separate the jaws, to prevent trauma to the tongue, to allow aspiration of retained saliva, and to permit the maintenance of oral hygiene, a modified dental prop or an oropharyngeal airway is sometimes tried. But the presence of one of these, except in deep coma, can provoke further spasms, increase salivation, prevent swallowing, or may initiate laryngeal stridor or, much worse, retching and vomiting.

Frank laryngeal spasm is obvious. Less obvious, yet more dangerous because of its insidiousness, is the slow progressive hypoxia arising from trismus, with retained naso-pharyngeal secretion. These difficulties, and many others, can be avoided by the safety bypass of a tracheostome.

(2) *Tracheotomy.* Early tracheotomy, as a prophylactic measure, is strongly advocated, particularly by those who have had experience of many patients (Godman and Adriani, 1949; Creech et al., 1950; Herzon et al., 1951; Saint et al., 1953). It should not be applied as a routine, but there should be no hesitancy in using it when indicated; in severe attacks it must be done early (Woolmer, 1953).

There is unfortunately a conservative attitude on the part of many to this operation, even in the presence of specific indications. In tetanus, this conservatism is no longer justifiable (Saint, 1953). Undue delay will jeopardize the patient's life from sudden spasm, complete exhaustion, or dangerous hypoxia. An unnecessary strain is thrown both on the patient and on those fighting for his life.

In the following list of indications, each relevant factor must be considered in association with the general condition of the patient, the success or otherwise of the treatment, and the severity and stage of the disease.

(a) *Indications for tracheotomy in tetanus.*

(1) Prophylactically, when the disease is likely to be severe, with the early and rapid onset of severe spasms.
(2) Reflex spasms which cannot be adequately controlled by treatment with sedatives.
(3) Unrelieved trismus or gross oedema or trauma of the tongue.
(4) Disorganized swallowing, with pooling of saliva, or danger from retching and vomiting.
(5) Laryngeal disorganization, with stridor, obstruction or oedema, and absent cough reflexes.
(6) Pulmonary stagnation, atelectasis or pneumonia.
(7) Prolonged unrelieved spasm of the respiratory muscles, interfering with efficient pulmonary ventilation.
(8) Paralysis from muscle relaxants.
(9) Deep coma from over-sedation.

(b) *The operation.*

Tracheotomy, through the second or third tracheal ring, can be more easily performed as an elective operation under endotracheal anaesthesia. Galloway and Wilson (1955), advise a rapid induction with an intravenous barbiturate; relaxation with a neuromuscular blocking agent, e.g., suxamethonium; oral intubation with a cuffed tube; and maintenance with nitrous oxide-oxygen anaesthesia.

For the emergency relief of obstruction, oral intubation under relaxant cover is to be preferred to a hurried tracheotomy. An elective operation can be done later, but oral tubes should not be left in place for longer than 12 hours because of the danger of ulceration of the vocal cords, or of the trachea in the subglottic region (Gusterton, 1955).

In patients for transfer, tracheotomy is more conveniently done at the receiving hospital. When any danger from asphyxia might arise during transfer, a preliminary oral intubation should be done.

(c) *The choice of tracheotomy tube.*

The type of tube will depend on the reason for the tracheotomy. (1) The standard silver tube with fixation flange is adequate for those patients in whom a free or alternative airway is all that is required, and in whom there may be no danger from pharyngeal aspiration. Sometimes, a smaller tube can be used, with the central blocker kept in place, this being removed only for suction purposes or as an emergency airway. In such cases breathing occurs round the tube and humidification problems do not arise. (2) The cuffed rubber tube will be required in patients with laryngeal disorganization to prevent aspiration; or when intermittent positive pressure respiration (I.P.P.R.) is contemplated.

The rubber tube commonly used is a standard endotracheal cuffed tube, shortened in length to approximately 3½ inches, cut and chamfered just distal to the cuff, and fitted with a Cobb's suction union.

This standard tube has certain disadvantages. Fixation of the external end without a suitable flange can be difficult, especially when connected to respiration apparatus. Kinking may occur with complete or partial obstruction of the lumen. Insufficient curvature of the tube may exert undue pressure on the posterior wall of the trachea, while over-inflation of the cuff will cause mucosal ischaemia leading to ulceration. A long tube may pass into a bronchus, especially if the tracheostome is too low.

There is no satisfactory tube to meet all these objections. Rubber angular tubes have been tried, of which the Swedish Sjoberg tube is an example. Hodges et al. (1956) used the outer shell of a standard silver tube and slid this inside a cut down rubber cuffed tube, with the angle of the silver tube above the cuff. Careful selection is important, but this modification, made from apparatus in common use, overcomes many of the troubles that may arise.

(d) *Management.*

Two serious complications, infection and drying up of secretions, can follow tracheotomy.

(1) *Prophylaxis of infection.* Careless technique is responsible for much of the tracheobronchitis that occurs, so often associated with an antibiotic-resistant pathogen. The importance of strict asepsis must be impressed on nurses, and tracheal catheters must be kept separately from nasal and pharyngeal suckers.

Too vigorous and too powerful aspiration can cause extensive damage to the delicate tracheal mucosa. Tracheobronchial toilet must be done as gently as possible, and a side hole, or Y-tube, incorporated in the suction holder to prevent too high a build-up of negative pressure. Plum and Dunning (1956), reporting on 8 postmortem specimens removed from patients who had died within one and a half to four days after tracheotomy, found extensive haemorrhage and ulceration of the trachea and right bronchus due to careless and vigorous suction.

(2) *Humidification.* The drying up and crusting of the tracheobronchial tree that can follow tracheotomy may become so serious as to jeopardize the purpose of the operation, and the patient's life. Secretions, initially increased, become so thick and tenacious that ciliary action ceases, suction is ineffective, and a viscid mucus cast may form, restricting the lumen and blocking the bronchi. Such a complication is prevalent in patients with absent cough reflexes.

Humidification of some sort is essential. The problem is to ensure that the air or gases inspired through the tracheotomy are already at body temperature and fully saturated. The time-honoured technique of bubbling gases through hot water in a Woulfe's bottle is not very effective, while the conventional steam kettle, tent or humidified room, to be at all efficient, makes conditions unbearable for both patient and staff.

The "Radcliffe" humidifier, developed by Marshall and Spalding (1953), is an excellent apparatus. Designed primarily for positive pressure respiration techniques, it can be adapted for spontaneous breathing by placing a special plastic bag over the free end of the tracheotomy tube and blowing the warmed humidified air from the apparatus into it (Crampton Smith et al., 1954). Alternatively, a modified Ayre's T-piece can be attached to the tracheotomy tube, with one arm connected to the humidifier and to the other a short piece of wide bore tubing open at the distal end. In either case the patient can breathe a mixture, which can be varied, of warmed humidified air and ordinary room air. The disadvantage is that more apparatus—a respiration pump or cylinders—is required to deliver the air or gases to the humidifier.

(e) *The advantages of Tracheotomy in Tetanus.*

(1) It provides a reliable airway, bypassing the sites of obstruction.

(2) It provides ease of aspiration of the tracheobronchial secretions.

(3) It allows efficient pulmonary ventilation, natural or applied, and is essential in I.P.P.R. techniques.

(4) It can prevent aspiration of saliva or vomit if a cuffed or closely fitting tube is used.

(5) It reduces the frequency and violence of the spasms (Galloway and Wilson, 1955), as increased respiratory effort, especially in the presence of obstruction, is itself a stimulus to reflex spasms.

(6) Less sedation is required (Saint, et al., 1953, and others).

(7) Oxygen consumption is lowered, because the accessory muscles of respiration need no longer be used to overcome the restricted airway (Pitman and Wilson, 1955).

(8) Both the patient and the nursing staff are to some extent, relieved of anxiety and strain.

2. *The Prevention of Obstructive Pulmonary Complications.*

The most common complication is atelectasis, that is, collapse of the lung distal to a block in a bronchus. It may be segmental or lobar and usually it is preventable.

The active co-operation of the patient with severe tetanus is generally not possible and breathing exercises are difficult to apply; other more active measures are necessary to loosen and drain the pulmonary secretions. The greater the severity of the disease, the more important these measures become. These are:

(a) *Postural drainage.* By this is meant the frequent change of position of the patient so that each part of the lung fields can be drained in rotation. The cycle is repeated every 2 to 4 hours, depending on the profuseness of secretions or on the tendency to atelectasis.

(b) *Chest physiotherapy.* The importance of the physiotherapist cannot be overemphasized. Her treatment supplies an artificial cough for her patient. Prophylactic therapy is essential from the onset. The principles of this treatment are firstly, clapping and percussion of the chest to loosen the secretions in the bronchioles, and secondly, expiratory vibration and shaking to squeeze loosened secretions into the larger bronchi and trachea, where they are more easily removed by ciliary action or by aspiration. Combined with postural drainage each lung is dealt with in turn and the treatment repeated as least twice daily, or more frequently if required.

(c) *Aspiration.* Where there is a tracheotomy, aspiration is done as often as necessary. Strict attention must be paid to gentleness and to asepsis.

(d) *Other measures* include frequent auscultation and daily radiological examinations of the chest.

*Comment.* These energetic measures, diligently applied, will keep the patient's lungs remarkably free. If they cannot be applied, either because of unrelieved tetanic tone in the respiratory muscles or for fear of evoking reflex convulsions, it would appear that the form of treatment being given for the tetanus might be basically unsound, especially if pulmonary complications develop.

*Treatment of Atelectasis.*

(*a*) An intensification of the general prophylactic regime with particular emphasis on the collapsed lung is the most important therapeutic measure. The turning routine is modified to allow free drainage of the affected part.

Chest physiotherapy must be really vigorous, and as this may stimulate reflex spasms in a patient not fully controlled, increased analgesia, or better still anaesthesia plus relaxation, may be necessary. Abolition of the tetanic tone in the respiratory muscles is an essential aid to success. These vigorous methods are repeated frequently, even hourly, until the offending mucus plug has been dislodged, and the lung expands.

(*b*) Bronchoscopy. If physiotherapeutic methods fail, bronchoscopy should not be unduly delayed. Its use should be considered a reflection on the preventive regime. It is best done under general anaesthesia, with additional relaxation, and through the mouth rather than through the tracheostome (Crampton Smith, 1955).

(*c*) Other measures. Where secretions are thick and tenacious, humidification (even without a tracheotomy) may be of considerable help; the instillation of sodium bicarbonate or, more recently, the use of "Alevaire" and enzymes, such as trypsin, by aerosol may be of value.

3. *Prevention of Lung Infection.*

The prophylactic and therapeutic use of the antibiotics has reduced the incidence, morbidity, and indeed the mortality of lung infection.

### (3) CONTROL OF REFLEX SPASMS AND TONIC RIGIDITY

*Introduction.*

Until recent years sedation had been the only form of treatment. Formerly, as the disease progressed, so more sedation was required, and the induced coma, or its complications, often proved fatal.

Although curare had been tried, notably in 1935 (Cole, 1935; West, 1936) the "relaxant era" did not start until the middle 1940s, and for the next few years the various drugs in this group, combined with the sedatives, were tried in many patients. Some reports were enthusiastic, but in many of these the prognostic histories were already favourable. Other reports cast much doubt on their benefit. Many emphasized the difficulty of achieving sufficient release of the excess muscle tone without producing respiratory depression, while occasionally their use seemed to hasten the end.

In 1952 there were two important developments. Firstly, *intentionally induced total paralysis* was combined with *artificial respiration*, an anaesthetic technique already common practice in the operating theatre. Van Bergen and Buckley (1952) in America are credited with being the first to apply this principle. They saved a 5-year-old child with severe tetanus, moribund from heavy sedation, by inducing complete curarization, combined with artificial respiration; they maintained this for 6 days, no further sedatives being required. This report received little attention at the time, and it was not until the spectacular success was published of I.P.P.R. methods, applied to the many paralysed poliomyelitis patients in Copenhagen in 1952, that the importance of this new principle was realized.

The second development was the rapid increase in knowledge and experience in the long-term management of the paralysed patients gained in that epidemic and to which Lassen (1953) and Ibsen (1954) have contributed so much.

This technique of induced total paralysis, so simple in concept yet fraught with many technical difficulties, should reduce the mortality in tetanus to almost nil (Russell et al., 1955). Hitherto, in the severe forms, death might have occurred within a few days. The application of this new principle together with conventional methods of treatment should prevent many deaths from the more common complications of this disease. With life prolonged it may reveal that a proportion of patients may develop new complications or die from other possible effects of the toxin (Bodman, 1954). Such untoward effects already have occurred, notably from depression of the bone marrow. (Fatal agranulocytosis—Lassen et al., 1954; Gormsen, 1955; and the author and his colleagues.)

More recently Kelly and Laurence (1956) have stressed the impracticability of the total paralysis regime in countries where tetanus is common and skilled anaesthetists few. They and others (Bodman et al., 1955; Cole and Robertson, 1955; and others) have found chlorpromazine a drug of some promise.

Meanwhile Forbes and Auld (1955) have published an impressive series of 15 consecutive cases of tetanus *with no deaths*, all being treated *with sedatives alone*.

It would appear that treatment has turned a

complete circle. In so doing, the concept of "totality of endeavour" (Forbes and Auld, 1955) has become foremost, with particular attention paid to the problems of the airway and the maintenance of adequate respiration.

Tetanus is such a variable disease that an accurate assessment of any form of treatment can be hard to make. Undoubtedly some patients will survive with sedation alone; in others a combination of drugs might be more suitable, while in a few the logical and diligent application of induced paralysis would seem to offer the best chance of recovery.

There are, therefore, two principal methods of controlling reflex spasms; the use primarily of sedatives, with or without additional relaxation, and the use primarily of the muscular relaxants with light anaesthesia or mild sedation.

1. *Sedation*: (a) *The Sedatives.*

Sedation—"the keystone of treatment" (Forbes and Auld, 1955)—is essential to relieve anxiety, to induce sleep, to lessen exhaustion, and to reduce the incidence of reflex spasms. Large doses may be required even when spasms are absent or only mild and infrequent. As the disease progresses, heavier sedation may become necessary, with the risks of deep coma. Van Bergen and Buckley's (1952) patient, previously quoted, is an example of the overdose that may result from efforts to control the severe convulsions, with sedation alone, and an example, too, of how such a moribund patient can be saved.

The sedatives in common use, for example the barbiturates, paraldehyde, and chloral, have little effect on the gross muscle rigidity, except in excessive doses. In such doses they are all central depressants. They act on the basal ganglia and medullary centres; so does hypoxia from deficient pulmonary ventilation or a restricted airway; so does the tetanus toxin (Baker, 1942, 1943; Woolmer, 1954).

The severity of the spasms and the degree of hypertonia vary unpredictably, and in maintaining a patient free from dangerous spasms and relieved of some of the excess tone by sedatives alone the level of sedation may be barely sufficient at one moment, yet excessive the next. To avoid this risk of overdose a combination with drugs such as mephenesin or chlorpromazine, separately or together, might be more effective. If adequate control still cannot be safely achieved, the regime of induced paralysis (see later) should be implemented if facilities allow.

Cumulative and toxic drugs are better avoided. Routine set-interval administration (every three hours, for instance) can also lead to accumulation; each dose can be carefully assessed. Phenobarbitone, to provide a basal sedation, has the advantage of infrequency of administration, but paraldehyde or the medium-acting barbiturates (sodium amylobarbitone, pentobarbitone) are more satisfactory. A short-acting drug such as thiopentone in continuous infusion can provide a more immediate and flexible control, especially when combined with a basal sedative.

Grant and McNeilly (1953) successfully used continuous thiopentone 0.4 per cent in a patient aged 20, without tracheotomy. They found that 1.0 g thiopentone was required every 7 hours, and this, combined with pethidine 100 mg 6 hourly, was continued for 16 days. On the second and fourth nights of this treatment there were major crises in which severe spasms were followed by inhalation of regurgitated stomach contents. On each occasion the youth was intubated and large quantities of mucus and gastric contents were aspirated.

A boy aged 7 (Batten, 1956) was successfully treated with thiopentone 1.5 per cent at a daily average of 2.25 g per day for 15 days without tracheotomy. Trismus persisted throughout, and tonicity varied from full opisthotonus to mild tightness while "several attacks of laryngeal spasm caused cyanosis".

These examples illustrate the precarious state of the patient if undue, some would say unnecessary, risks are taken. Over-emphasis of one aspect (sedation), neglect of another (the airway), of the therapeutic or prophylactic measures, may well compromise the patient (Forbes and Auld, 1955). For instance, a boy aged 9 with a period of onset of only 21 hours (Bodman et al., 1955) was being treated with chlorpromazine and nitrous oxide anaesthesia when, after 12 days of hard battle, a sudden severe convulsion asphyxiated him, and he died. Tracheotomy had been considered but not done, partly for fear of the known complications of this operation.

(b) *Chlorpromazine.*

Experimentally, Hougs and Anderson (1954) found that either chlorpromazine (1 mg/kg of

body weight) or promethazine (1 mg/kg) injected intravenously could abolish local tetanus in rabbits. Kelly and Laurence (1956) have confirmed these findings (though promethazine—4 mg/kg—had a weaker action), while Dasgupta and Werner (1955) suggested that chlorpromazine has an action on the spinal cord similar to mephenesin.

Clinically, using chlorpromazine *alone*, Kelly and Laurence (1956) successfully treated a child of 2½ years with severe tetanic spasms. The dose varied from 15 mg (1 mg/kg) to 40 mg as single intravenous injections every 2 to 5 hours, while the total reached 330 mg in one 24-hour period. A total of 3,145 mg was given in 16 days, the aim of the treatment being to subdue the spasms, rather than to achieve complete relaxation. There was no tracheotomy, and several cyanotic episodes from convulsions occurred.

Cole and Robertson (1955), in Tanganyika, found chlorpromazine in 50 mg doses, by injection, *combined with sedation* (phenobarbitone 3 grains) useful in inhibiting seizures, the effect lasting 8 to 12 hours. Both they and Kelly and Laurence offer no opinion as to its effect on mortality or its place in treatment.

Bodman et al. (1955) combined chlorpromazine, pethidine, and promethazine, given separately in 25 mg doses every 4 hours, *with nitrous oxide oxygen anaesthesia*. This controlled the convulsions without impairing adequate spontaneous respiration. Withdrawal either of the nitrous oxide or of the chlorpromazine resulted in the reappearance of the convulsions.

Anderson et al (1955) used chlorpromazine 25 mg, 6 hourly for 36 hours, and then *combined it with induced total paralysis* using curare, I.P.P.R., and nitrous oxide anaesthesia through a tracheotomy. This regime was maintained satisfactorily for 12½ days, when all treatment was withdrawn except the nitrous oxide. Four and a half days later there was a sudden resurgence of "cyanotic spasms" due, it was thought, to secondary tetanus. Total paralysis was re-instituted, but death occurred 3 days later from agranulocytosis (Gormsen, 1955).

Adriani and Kerr (1955) combined *chlorpromazine with mephenesin and barbiturates* in 11 patients, with 5 deaths. Finally, the use of *"artificial hibernation"* has been reported from many Continental centres with mixed results.

The advantages claimed for chlorpromazine are:

(1) Euphoria replaces acute anxiety.

(2) Coma is not deep (Kelly and Laurence, 1956).

(3) The site of action, though central, is at a different level from that of the narcotics.

(4) Reflex spasms can be inhibited.

(5) Hypertonia can be reduced without central respiratory depression.

(6) Secretions (sweat, salivary, pulmonary) are reduced.

(7) Metabolism is lowered.

(8) The action of the hypnotics, mephenesin, and the relaxants is potentiated.

*Comment*. The present position is that, like the sedatives, chlorpromazine alone has limited application in the more severe case. It may be of value when combined with other drugs or groups of drugs, and examples of some possible combinations have been given above. Toxic reactions, especially jaundice and agranulocytosis, have been reported; an assessment of the drug cannot yet be made.

2. *The Muscular Relaxants.*

(a) *Drugs with a central action – Mephenesin.* Mephenesin, introduced by Berger and Bradley (1946), has a central action depressing reflex excitability. The sites of action are on the internuncial cells and neurones in the spinal cord and the reticular bulbar formation in the brain stem (Henneman et al., 1949; Kaada, 1950). The polysynaptic reflexes are depressed with small doses, the monosynaptic reflexes only with larger doses (Taverner, 1952). The drowsiness and nystagmus that occurs with heavy doses suggest an action higher still in the brain stem (Kelly and Laurence, 1955). There is also a definite but important (from the swallowing viewpoint) local analgesic action when applied directly to the pharynx and larynx (Newhouse et al., 1950). All actions are of short duration.

Clinically, it produces a muscular relaxation without respiratory depression, except in excessive doses. Its use in tetanus was first suggested by Belfrage (1947).

*The advantages of mephenesin in tetanus.*

(1) It overcomes hypertonia, and relieves the pain from muscle spasm.

(2) It increases the vital capacity and allows the conscious patient to do active breathing exercises, even to cough.

(3) Trismus is relieved and normal swallowing becomes possible.

(4) It reduces the violence of the spasms but it does not prevent them. It may reduce their frequency when combined with sedation.

(5) It has a wide margin of safety, the first signs of overdose being diplopia, nystagmus, and drowsiness.

(6) By intravenous infusion, a continuously controlled relaxation is possible.

(7) It can be given intravenously, intramuscularly, orally and rectally.

(8) It is non-cumulative.

*Disadvantages.*

(1) *Intravenously,* its action is transient, the effect lasting some 30 to 45 minutes following a single injection. Intramuscular injection may last a little longer.

(2) Concentrations above 4 per cent may produce venous thrombosis, or intravascular haemolysis leading to haemoglobinuria (Pugh and Enderby, 1947). (The commercial ampoule contains 1 g in 10 ml of a solution containing alcohol.)

(3) Temporary hypotension sometimes occurs, possibly from overdose (Gammon and Churchill, 1949; Smith, H., 1953; Taverner, 1952).

(4) The oral preparations should not be given by mouth when dysphagia is present; administration by indwelling intragastric tube is preferable. Undue delay in swallowing mephenesin, whether as elixir, powder, tablets or suspension, may result in pharyngeal or laryngeal analgesia, with possible inhalation of saliva and food.

(5) Nausea and gastritis are common when high doses are given; the elixir, which contains alcohol, can produce a drunken stupor, particularly in children.

*Dosage.*

In the normal conscious subject an intravenous injection of 30 mg/kg of body weight (200 mg/stone) produces a generalized muscular relaxation with sometimes a little respiratory depression.

In the tetanic subject higher doses may be necessary. The aim in mephenesin therapy is to relieve some or all of the excess muscle tone. For a continuous effect an intravenous infusion of a 1 to 1.5 per cent solution is the most satisfactory method, the concentration and drip rate being adjusted to maintain the desired effect and to suit fluid requirements.

*Examples.*

Recent reports have shown a much heavier dose used than formerly, and in the following examples a continuous infusion was used: Davison (1951) in a boy of 13 years used 91 g. in 6 days; Laurence (1952) quotes a child of only 1½ years in whom 37 g. were given in 3 days (i.e., approximately 40 mg/kg/hour); Docherty (1955) in a youth aged 16 used 198 g. in 14 days.

In a boy aged 13, with a period of onset of 7 days and an approximate weight of 35 kg (5½ stone), 386 g. were successfuly infused in 13 days by the author and his colleagues, an overall average of 1.25 g./hour (35 mg/kg./hour) with a maximum 24-hour total of 40 g. (46 mg/kg/hour). At this dosage there was a mild sedative effect with no depression of respiration, and reflex spasms were mild and infrequent. Without mephenesin there was gross tetanic rigidity, pain, sweating, and fairly frequent spasms of variable severity. The oral preparations were tried during the acute phase but to achieve comparable conditions they caused nausea or, with the elixir, a drunken stupor. They were used successfully at a smaller dosage in the convalescent stage.

*Comment.* The overriding disadvantage of mephenesin is its brief action. The high dosage frequently required usually necessitates a continuous infusion to avoid the gastric disturbances caused by the oral preparations. The oral route is suitable only for the mild case or the convalescent stage of the more severe, by indwelling gastric tube if there is any dysphagia.

(b) *Peripheral Neuromuscular Block.*

The relaxants such as curare and gallamine often caused depression of respiration and their use frequently proved disappointing. Subsequently, the method of induced *relaxation* with assisted respiration was advocated, with suxa-

methonium as the drug of choice, since a continuous infusion (0.1 to 0.3 per cent) could be adjusted to follow the minute-to-minute variations in the hypertonia (Woolmer, 1953, 1954).

As an example, a woman aged 58 required a dose of 2.5 mg/min in the acute phase to produce some relaxation without affecting breathing, yet later only 0.2 mg/min caused respiratory depression with cyanosis, requiring pulmonary inflation with oxygen (Woolmer and Cates, 1952). Brinton and Burk (1955), in a man aged 54, found 5 mg/min necessary during periods of hyperexcitability, yet paralysis was not complete. Their patient was unsedated, and although on artificial respiration in a Drinker apparatus, he was able to indicate the rate of drip which varied from 200 to 300 mg/hr of scoline, later falling to 160 mg/hr. They gave 28 g. in 6 days. Both examples illustrate the higher dosage required during the acute stages of the illness.

Though physiologically more correct, this method might be difficult in prolonged treatment. More recently, induced *total paralysis* with artificial respiration has become an established method, and this highly specialized technique is indicated when other methods fail to control severe spasms, though it can make considerable demands on the expert staff and the ancillary services of the hospital.

*The "Total Paralysis" Regime.*

The essentials of the induced *total paralysis regime* are: (1) tracheotomy, with a cuffed tube (previously discussed); (2) induced paralysis; (3) I.P.P.R.; and (4) minimum sedation.

*Induced Total Paralysis.*

*The Longer-acting Group—Curariform Drugs.* Curare has several advocates (Lassen et al., 1954; Honey et al., 1954; Anderson et al., 1955; and others). The advantages claimed are that the return of muscle tone is slow (a rapid return is unnecessary); intramuscular injection is effective and "depot" forms in a wax base ("Tubadil") may be advantageous. Intravenous infusion for injection purposes, though preferable, is not essential. Overdose, provided I.P.P.R. is adequate, carries no material risk.

The disadvantages are that repeated injections are required and a waxing and waning in the degree of paralysis can occur, which can affect the efficiency of a mechanical respirator. The cumulative effect of curare can cause considerable delay in the return of sufficient spontaneous respiration. One patient aged 42, who received 1,005 mg tubocurarine chloride and 350 mg Tubadil in 6 days, took 24 hours to regain adequate respiration following cessation of the curare to assess progress during treatment (Honey et al., 1954).

*The Short-acting Group—Suxamethonium.* 22.5 g. of suxamethonium, in a continuous infusion, was used by Forrester (1954) in 5½ days (3 mg/min) of total paralysis, with *manual* inflation of the rebreathing bag, supplemented with nitrous oxide-oxygen anaesthesia.

Employing *mechanical* inflation, the author and his colleagues found that a profound paralysis was necessary. In a youth aged 15 years, with a period of onset of 30 hours, they successfully used 77 g. of suxamethonium in 11 days of total paralysis, 7 to 8 mg/min being required in the acute stages; it was supplemented throughout with nitrous oxide anaesthesia, with to-and-fro carbon dioxide absorption, and intermittent pethidine.

The disadvantages of continuous suxamethonium are that failure of the infusion may result in a rapid and undesirable return of muscle tone; succinyl monocholine may be produced (Collier and Macauley, 1953); salivary and bronchial secretions may be increased; and the blood pressure may be unduly sensitive to variations in pulmonary ventilation.

*Intermittent Positive Pressure Respiration (I.P.P.R.).*

*Manual* inflation, for emergency use, is essential. For long-term treatment, it can be difficult to maintain constant respiratory rates and volumes; it is laborious and dependent on the availability of relays of human volunteers whose "inflating" efficiency can be most variable. "Assisted" respiration would be even more technically difficult to apply over long periods.

*Mechanical* means of inflation, recently reviewed in this Journal (Mushin and Rendell-Baker, 1954), provide a more controllable and uniform pulmonary ventilation. There are two main groups of apparatus; those primarily for use

with anaesthetic circuits (Aintree, Fazakerley); and those which can inflate the patient with air and are independent of anaesthetic apparatus (Beaver, Radcliffe Respiration Pump).

With mechanical inflation, a complete paralysis is desirable, for any increase in the resistance to inflation may not be compensated by a pulmoflator set at constant inspiratory pressure. A fall in the respiratory minute volume would result, causing carbon dioxide retention. Such a condition can be due either to returning muscle tone, in which case more relaxant would reverse these effects; or to the development of obstruction (atelectasis) within the pulmonary tree, when further relaxant would have no effect, since a greater pressure is required to inflate the diseased chest in a patient totally paralysed (Spalding, 1955; Spalding and Young, 1955).

Constant and physiologically correct ventilation is not easy to maintain in paralysis from disease; it can be even more difficult under the artificial conditions of induced paralysis. As a guide to efficient pulmonary exchange, the following should be observed, where applicable:

(*a*) Colour changes in the skin.
(*b*) Incidence of sweating.
(*c*) Changes in the size of the pupil.
(*d*) Frequent pulse and blood pressure recordings (½ hourly).
(*e*) Frequent measurements of minute volumes, and of $CO_2$ in the expired air.
(*f*) Inflationary pressure readings.
(*g*) Oximetry measurements.
(*h*) Daily urinary pH.
(*i*) Daily blood biochemistry.

*Sedation, with Total Paralysis.*

With convulsions fully controlled, only the minimum of sedation is necessary; light anaesthesia can be used or the sedatives, or a combination of both, depending on the method of I.P.P.R.

*Nitrous oxide* is noncumulative and rapidly eliminated, but additional hazards are introduced, anaesthetic apparatus is necessary, and because the gas is expensive, carbon dioxide absorption is desirable. In semiclosed circuits there may be a frequent incidence of atelectasis due to the rapid absorption of the gases from the alveoli should a bronchial block occur. The author and his colleagues have found that the addition of *nitrogen*, which is slowly absorbed, to the mixture reduces the incidence of atelectasis.

*The sedatives* are usually required when the air respiration pumps are used. For instance, Honey et al. (1954) employing the Radcliffe pump, used sodium amylobarbitone 200 mg every 4 hours supplemented by thiopentone.

It may be difficult to assess the level of consciousness or of coma in the patient completely paralysed. E.E.G. recordings may be of some help. These authors mention that "large amounts of barbiturates may be required and the immediate danger of barbiturate poisoning—namely respiratory arrest—is eliminated, since respiration is controlled".

Additional central depression of the medulla in the severely ill patient would appear undesirable. Some anaesthetists prefer a method such as nitrous oxide anaesthesia which, despite its admitted disadvantages, is flexible. Combined with mild basal sedation and with pethidine as an analgesic, the risk of overdose with any one drug might be reduced.

### (4) THE MAINTENANCE OF STRENGTH AND FLUID BALANCE

Tetanus is an exhausting disease, with a raised metabolic rate (Holmdahl and Thorén, 1954), and with excessive loss of fluid from sweat and saliva. Nutrition as well as fluid and electrolyte balance should be carefully maintained since treatment may be prolonged and the convalescent stage of "residual tetanus" difficult (Wilson and Care, 1955).

*Feeding by mouth should be avoided* as it can be dangerous in the presence of dysphagia. Some rely on parenteral feeding alone (Forbes and Auld, 1955) because of the ever present danger of gastric regurgitation, though this complication can be minimized with a cuffed tracheotomy tube; with such a tube nutritional and fluid needs can be better supplied, either by an indwelling nasal intragastric plastic tube or by a *Kader Senn gastrostomy*. High daily calorie intake (2,000 to 3,000 calories) is required by frequent small volume feeds or by continuous drip. A constant watch should be kept on fluid and electrolyte

balance with biochemical analyses of blood, daily if necessary, and changes in the haemoglobin content or red cell count of the peripheral blood should be corrected.

### (5) ORGANIZATION

Recovery is complete in those who survive. Much will depend on good nursing, attention to detail, and adequate facilities. The application over long periods even of the regime of sedation, parenteral feeding and tracheotomy advocated by Forbes and Auld (1955) can make considerable demands on hospital staff. Even greater effort and vigilance is required when induced paralysis methods are used and for which specially trained teams are desirable.

These newer forms of treatment requiring the constant presence of the expert, especially the anaesthetist, may be impracticable in some hospitals; they should not be undertaken lightly. Special centres, examples of which are the Tetanus Unit at Leeds and the Respiration Unit at Oxford, are better equipped to deal with the complex problems that may arise.


### SUMMARY

1. A review is given of the symptomatology and treatment of tetanus.

2. The respiratory problems peculiar to the disease have been discussed and the methods of preventing the more common complications and causes of death are mentioned.

3. Emphasis has been laid on the importance of maintaining a clear airway and effective pulmonary ventilation.

4. Tracheotomy as a prophylactic measure is advocated in all severe cases and its specific indications and management are discussed.

5. The different forms of treatment with sedatives, chlorpromazine, mephenesin, and induced paralysis are reviewed.

6. Treatment in all but the mildest cases consists of a carefully integrated therapeutic regime demanding constant vigilance, adequate staff, and full hospital facilities.


### ADDENDUM

Since this review was written, Lassen et al. (1956) have published some important observations on the possible toxic effects on the bone marrow from *continuous* nitrous oxide anaesthesia. Quoting two cases of fatal agranulocytosis following its use (Lassen et al., 1954; Gormsen, 1955), they published a third fatal case, and also report two further patients in whom, after 5 days of continuous nitrous oxide, severe leucopenia and thrombocytopenia developed. In both patients, haematological remission occurred 3 days after the gas was discontinued. Bone marrow biopsies showed disturbance of granulocytopoiesis and "severe depression of erythropoiesis of the megaloblastic type", changes which they consider typical. In reviewing the treatment of 13 cases of tetanus, they found that in 6 who received continuous nitrous oxide, there were changes in the peripheral blood.

In this country, continuous nitrous oxide was used by Forrester (1954) and Bodman (1955), but no changes in the blood were reported. In cases as yet unpublished, the author and his colleagues used this agent with success (August, 1954) continuously for 11 days in one patient (previously mentioned) without ill-effects; but in another (September, 1955), treated initially with mephenesin and subsequently by total paralysis, marrow aplasia of the type described by Lassen (1956) occurred after 6 days of anaesthesia; this patient died on the twelfth day of treatment. A third patient aged 74 (April 1956), treated with mephenesin and chlorpromazine and *intermittent* nitrous oxide anaesthesia (for turning and chest physiotherapy), also developed a similar aplasia on the eleventh day of treatment; this patient also died.

Hitherto, nitrous oxide has been considered nontoxic. In view of these new complications, caution should be exercised in its prolonged use.

Whatever form of treatment is adopted, careful haematological control is necessary, since in severe tetanus, boldness may be required in pressing drug therapy to the limits of safety (Kelly and Laurence, 1956). Further experimental work is required to determine what these limits are.


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# QUESTION AND ANSWER

BY

P. R. BROMAGE

*Department of Anaesthesia, Royal Victoria Hospital, Montreal.*

*QUESTION*

For what therapeutic reasons is paravertebral injection performed? What complications may follow this procedure and how may they be prevented?

*Planning the answer.*

The examinee should allow ample time for answering the second half of the question, which is longer than the first. Notice that the question asks, "For what *therapeutic* reasons . . .?"; therefore, do not waste time discussing surgical indications.

*ANSWER*

Each paravertebral space contains a mixed spinal nerve emerging from the intervertebral foramen. In addition, the sympathetic ganglia and their connecting rami are present in the paravertebral spaces within the distribution of the sympathetic outflow ($T_1 - L_2$). A therapeutic paravertebral injection is indicated in any condition where it is necessary to interrupt one or both of these nervous elements for diagnostic purposes, or to relieve pain or to modify sympathetic activity. Aqueous solutions of local anaesthetics are usually employed, and repeated as necessary. In long-established painful conditions (e.g. intractable angina pectoris) it may be necessary to destroy the nerves concerned, and then alcohol is used.

Examples of indications for therapeutic paravertebral injection are as follows:

*Acute pain.* Multiple fractures of ribs, if pain is causing marked inhibition of respiration. In acute pancreatitis pain is relieved by paravertebral block of the seventh, eighth, and ninth thoracic nerves on both sides.

*Chronic pain.* Causalgia, angina pectoris.

*Sympathetic dystrophies.* Sudek's post-traumatic atrophy, reflex anuria, reflex vascular spasm (e.g. phlegmasia caerulea dolens).

The itching and vesiculation of herpes zoster can be improved if paravertebral sympathetic blocks of the involved segments are carried out in the acute stage, and then post-herpetic pain is unlikely to follow. But paravertebral blocks seldom produce lasting relief once the chronic stage of post-herpetic pain has been established.

Diagnostic paravertebral blocks are sometimes valuable in cases of vascular insufficiency of the limbs, in order to decide whether surgical sympathectomy is likely to be a worthwhile procedure.

*Complications.*

Sepsis is a possible complication of any injection, and so it is a sine qua non that all drugs and equipment should be adequately sterilized, preferably by autoclaving, and the block should be carried out under aseptic conditions. Treatment with anticoagulant drugs is a contra-indication to paravertebral injection, for puncture wounds of small vessels, which would normally be of no consequence, may ooze indefinitely, causing a large hidden haematoma and loss of circulating blood volume.

The most frequent complications are those arising from anatomical misplacement of the needle, or injected solution, into structures bordering on the paravertebral space. Intravascular injection of local anaesthetic solution into one of the many neighbouring blood vessels may lead to toxic convulsions. This accident can be avoided by careful and repeated aspiration; if blood enters the syringe the position of the needle should be altered until blood is no longer aspirated. If the needle is directed too far medially it may enter an intervertebral foramen and puncture the dural prolongation of a nerve

root, or even the main dural sac, and possibly injure the spinal cord itself. If a large amount of local anaesthetic is injected into the subarachnoid space a "total spinal" will result; this accident can be avoided by careful aspiration for cerebrospinal fluid. In the thoracic region, puncture of the lung, with resulting pneumothorax, is the foremost hazard to be avoided; this can only be prevented by accurate technique. The puncture should be made 1½ inches from the midline, and the needle directed forward and medially at an angle of 15° to the sagittal plane until the side of the vertebral body is struck. In difficult cases the position of the needle may be checked by anteroposterior and lateral radiographs.

Analgesic solutions can spread from one paravertebral space, through the intervertebral foramen, up and down and across the midline by way of the extradural space. Therefore, if large volumes of solution are used analgesia may extend unnecessarily far, and the resulting sympathetic paralysis may lead to hypotension. In the region of the seventh cervical and first thoracic segments the solution may spread too far anteriorly and involve the recurrent laryngeal nerve; therefore, care should be exercised if bilateral blocks are carried out in that area lest both vocal cords become paralysed.

Lastly, complications may arise from the nature of the injected solution. If excessive quantities of local anaesthetic are injected, rapid vascular absorption may lead to toxic convulsions and vasomotor collapse. Premedication with a barbiturate drug may diminish this danger slightly, but it is wise to keep the total quantity of local anaesthetic well within its toxic range, and to add a vasoconstrictor drug, such as adrenaline or noradrenaline 1 in 250,000 in order to delay vascular absorption. Therapeutic injections of alcohol sometimes give rise to "alcohol neuritis" of the affected nerves, and extensive spinal cord damage may result if alcohol is accidentally injected into the subarachnoid space; there is no way of preventing the former, but the latter must be avoided by careful technique. So-called "long-acting" solutions of anaesthetic base in propylene glycol are especially dangerous, these may cause a retrograde thrombosis of the spinal veins and arteries, leading to infarction of the cord: their use should be avoided.

## BOOK REVIEW

*Should the Patient Know the Truth.* Edited by Samuel Standard, M.D., and Helmuth Nathan, M.D. Springer Publishing Co., Inc., New York, 1955. Pp. 160. Flexible cover 15*s.*; bound 22*s.*

The subject of this symposium is one which is exercising very greatly the minds of medical men, as well as of ministers of religion at the present time. Appropriately, therefore, this book is styled "a response of physicians, nurses, clergymen and lawyers."

It is significant that numerous meetings are being held where doctors and clergy come together to pool their experiences, and try to find some satisfactory, practical and working arrangement to deal with the problem. Preparation for a future life is one of the crying needs of today, but the place for this should not be left to the deathbed. It is only by systematic and constant teaching from youth onwards that the fruit of a serene and hopeful outlook can be enjoyed by those who are about to pass the final ordeal of earthly existence.

This book offers advice from many points of view, is well written, and should promote serious thought in the reader which will help him to make up his mind as to what should be his own opinion about the matter. This is vital to the work of anyone who has charge of the sick. It is only by experience and the acquisition of all the relevant knowledge that can be provided that the best help can be rendered to those who are in so much need of assistance. This collection of essays is highly recommended.

*R. J. Minnitt*

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# THE EVOLUTION OF ANAESTHESIA

BY

M. H. ARMSTRONG DAVISON

"Without history, a man's soul is purblind, seeing only those things which almost touch his eyes."

## INTRODUCTION

A KNOWLEDGE of the history of anaesthesia has no commercial value for the practising physician, but it does have an immense cultural value. The medical student is too harassed by the need to pass examinations to find the time to obtain a liberal education, but a liberal education is essential for the proper intellectual appreciation and enjoyment of life. The history of medicine has close contact with the story of every science and art, for history is the cement which binds together all the varied activities of man. To study medical history is to make acquaintance with all the numerous subjects which comprise a liberal education, and such study is thus a short cut to a knowledge of the humanities.

The history of anaesthesia is a large subject; paradoxically, it is also true that it does not exist at all. Anaesthesia is only a branch of medicine, and its history can only be understood by examining the whole subject. Equally, medicine is a branch of science, while science is only one facet of human activity: it follows, therefore, that the history of anaesthesia can only be interpreted correctly by viewing it in the perspective of other human activities, medical, scientific, and social; inventions, discoveries, wars, religious beliefs, and all the manifestations of art and culture.

The basic facts of the history of anaesthesia can be ascertained from books and papers which are within the province of all, but it is not everyone who is in a position to draw conclusions from these facts. Indeed the interpretation of history can only be undertaken by those who have considerable knowledge of many fields, and whose breadth of vision is therefore great enough to allow them to see the whole landscape, without being distracted by a few features, themselves dramatic enough, but which may, nevertheless, be of small importance in an appreciation of the nature of the whole terrain.

It is unfortunate, therefore, that the history of anaesthesia has been mainly considered by anaesthetists, for it is natural that they have viewed the field with nothing but their own subject in mind, and have therefore emphasized unduly a number of early attempts at pain relief, without considering whether these attempts have any causal relationship to the discovery of surgical anaesthesia.

Naturally, also, we tend to project our own humanitarianism into the minds of our progenitors, even as far back as the dawn of history. If one examines any book or chapter which tries to cover the history of anaesthesia, one finds some such statement as "From earliest times, man has sought to prevent pain." At first sight, this seems a reasonable remark; on consideration, however, it begins to appear less reasonable. Direct evidence is obviously lacking, but indirect evidence is often in flat contradiction. We have only to look back 200 years, and we see that the general tendency of mankind was to inflict pain, not to prevent it. The social history of England at that time discloses a treatment of malefactors, of lunatics, of slaves, and of animals which was barbaric in the extreme; and there is no reason to believe that uncivilized people are less brutal than we were in England at a date when the arts flourished more luxuriantly than at any other period in our history.

This is not to say that there were no humane beings, that no one prior to the end of the eighteenth century ever tried to prevent pain or to discover some means of surgical anaesthesia. Such people undoubtedly did exist, but their efforts produced no noticeable effect on the general attitude of their professional colleagues; they did not influence history and their work had no part

in the ultimate discovery of anaesthesia; they sank into oblivion from which some of them have only been rescued since anaesthesia became an accomplished fact.

For example, we are interested to know that Severino of Naples employed refrigeration analgesia for the operation of perineal lithotomy in the first half of the seventeenth century, but his technique passed almost unnoticed, and was not at all a factor in the recent reintroduction of refrigeration analgesia for amputation. None of the authors of the histories of anaesthesia seem to be aware of this important distinction: every event with the slightest anaesthetic flavour is seized on as part of the "history of anaesthesia", such as, for example, the story from Herodotus (fifth century B.C.) of the Scythians intoxicating themselves with the fumes produced by burning some sort of hemp (*History*, Book 4). This is obviously an attempt to make bricks without straw; the incident may have some anthropological importance, but it has no real bearing on the history of anaesthesia.

History teaches us that man has usually been tolerant of pain, especially in others; and this is very natural. Pain and disease were present long before man appeared on the earth, and the earliest man therefore accepted the ills to which the flesh is heir as a natural concomitant of life. The revolt against disease was slow: that against pain was slower still. It was not until the second half of the eighteenth century of the Christian era that a new feeling spread abroad. Humanitarianism became widespread among civilized peoples; while hitherto it had been a tender plant, rarely seen and often disregarded, it now grew to be the most important vegetation in the moral jungle. It was then that the history of anaesthesia began, nor was it long before anaesthesia itself came into being. The Renaissance had done its finest work: humanitarianism, the dislike of pain and suffering, was quickened into full life by the outwardly hateful events of the Industrial Revolution. Already the revival of learning and the development of experimental science had prepared the way; as soon as anaesthesia became a moral necessity, and knowledge and the tools being available, the discovery could not be long delayed. So the stage was set for that memorable day, October 16, 1846, when William Thomas Green Morton gave anaesthesia to the world.



### THE WORD "ANAESTHESIA"

The word "anaesthesia" is generally said to have been coined by Oliver Wendell Holmes; certainly he applied it to "etherization", but the word was already in current use before Morton's discovery.

Experimental science may be said to begin with Thales of Miletus (*c.*624–*c.*565 B.C.). This Ionian Greek had studied Mesopotamian and Egyptian astronomical and physical observations: he took a tremendous step forward when he used these observations to make deductions, and to argue from the particular to the general. Thus the empirical Mesopotamian astronomical knowledge led him to predict an eclipse of the sun, visible at Miletus in 585 B.C.; similarly, the Egyptian knowledge about special right-angled triangles (those with sides in the proportions 3:4:5: units of length, which the Egyptians used for constructing right-angles in their building operations) enabled him to deduce the general law expressed in the so-called Theorem of Pythagorus. Thus science began; the study of science was a peculiarly Greek gift to mankind. In the years after Thales, Greek science rose to tremendous heights, which, in spite of the Dark Ages, left us a legacy which we still enjoy. It is natural therefore, that the scientist turns to the Greek language when he wishes to record his observations and deductions. Hence it follows that scientific terms are almost entirely Greek in origin, and the words "anaesthesia" and "anaesthetic" are no exception.

The Greek stem *αἰσθε* means "to perceive" *ἀναίσθησις* thus means "an absence of feeling", and in classical times this conveyed a moral state, rather than a physical one, that is to say "a boorishness"; the word is used in this sense by Plato. It can still convey this meaning, although it is rarely used thus in modern times; for example, Windsor (*Ethica*, vii, 338) in 1860 uses the phrase, "this cold, anaesthetic temperament". During Roman times the great majority of physicians, even in the Eternal City itself, were Greeks, for the Roman genius turned more towards the work of the military surgeon. The

physicians naturally wrote in their own tongue, which was, in any case, the language of culture; but, with the passage of time, some words had changed in meaning. Dioscorides, who probably wrote at the end of the first or the beginning of the second century A.D., uses the word in its usual modern sense when discussing Mandragora. The *Shorter Oxford English Dictionary* dates the first use of the word "anaesthesia" in English as 1721; presumably it was then used to indicate loss of sensation in one limb or a part of the body. John Elliotson (*Numerous Cases of Surgical Operations without Pain in the Mesmeric State*, London, 1843, p. 65) quotes himself as using the word (from the context, in 1838) thus: "'For a length of time she had perfect loss of sense of touch,—anaesthesia, in her ecstatic delirium'." In June 1846, four months before Morton's successful demonstration of ether anaesthesia, Elliotson delivered an Harveian Oration, in which he used these words: "The loss of common feeling, —anaesthesia, is but a form of palsy, and in it wounds give no pain. If this condition can be induced temporarily by art, we of necessity enable persons to undergo surgical operations without suffering."

Morton attempted to keep secret the nature of the substance which he used; he therefore called it the "Letheon", a name suggested by Dr. A. A. Gould. The word is derived from the Greek, λήθη, oblivion; according to Latin poets, there was a river of this name in Hades; its waters were drunk by souls about to be reincarnated, and caused them to forget their previous existence.

Subsequently, on or about November 6, 1846, Morton revealed the nature of the substance confidentially to the authorities of the Massachusetts General Hospital, and on November 9, Dr. H. J. Bigelow read a paper at a meeting of the Boston Society of Medical Improvement, in which he stated that he had identified the Letheon with sulphuric ether.

Twelve days later, Oliver Wendell Holmes, at that time in practice in Boston, and the following year to be appointed Parkman Professor of Anatomy and Physiology and also Dean of the Harvard Medical School, wrote to Morton as follows:

November 21, 1846

Dr. Morton.

My dear Sir,

Everyone wants to have a hand in a great discovery. All I will do is to give you a hint or two as to names, or name, to be applied to the state produced, and to the agent.

The state should, I think, be called anaesthesia. This signifies insensibility, more particularly (as used by Linnaeus and Cullen) to objects of touch. The adjective will be an anaesthetic. Thus we might say the "state of anaesthesia", or the "anaesthetic state". The means employed would be properly called the "anti-aesthetic agent". Perhaps it might be allowable to say "anaesthetic agent"; but this admits of question.

The words, anti-neuric, aneuric, neuroleptic, neurolepsia, neurostasis, seem too anatomical; whereas the change is a physiological one. I throw these out for consideration.

I would have a name pretty soon, and consult some accomplished scholar, such as President Everett, or Dr. Bigelow, Sr., before fixing upon the terms which will be repeated by the tongues of every civilised race of mankind. You could mention these words which I suggest, for their consideration; but there may be others more appropriate and agreeable.

Yours respectfully,
O. W. HOLMES

There seems to be no evidence that further advice was sought. The words "anaesthesia" and "anaesthetic" were accepted readily by the profession, which was already familiar with them. Until the end of the nineteenth century, the original spelling was retained in America; early in the twentieth, however, the sensible simplified spelling "anesthesia", was introduced in the New World, and was fully established before the outbreak of the Great War. It is altogether unfortunate that, in the United States, the necessity for distinguishing between physicians and nurses who administer anaesthetics has led to the invention of the ugly words "anesthesiologist" and "anesthesiology". Both words are best avoided whenever possible.

### FURTHER READING

Many books have been written on the subject of the history of anaesthesia; the following notes may be helpful to the student who wishes to delve more deeply. A warning, however, is necessary: the student should guard himself against believing a statement simply because it is made in an authoritative manner; belief can only be commanded when a statement is supported by a satis-

factory reference, quoting an *original* document. Scepticism is the finest rein to the enquiring mind, and an attitude of honest scepticism should be cultivated. On reading a new statement, the student should say to himself, "I doubt that; what proof is offered?" If the proof seems adequate, qualified trust may be given, but the final acceptance of the statement as a *fact* depends on cumulative evidence, with no rebuttal. In identifying fingerprints, Scotland Yard demand that two prints, to be shown from the same finger, must have no less than sixteen points of similarity, and no single point of dissimilarity.

Books dealing with the history of medicine as a whole are valuable for filling in the background. As a general rule, these books deal with the history of anaesthesia in an unsatisfactory manner, but the following are strongly recommended.

*An Introduction to the History of Medicine* by Fielding H. Garrison. London, W. B. Saunders, 1913. This book reached its 4th edition in 1929 and has become recognized as the authoritative book on the subject. It is a work of reference rather than literature, and is well indexed.

*A Short History of Medicine* by Charles Singer. Oxford, Clarendon Press, 1928. A well-illustrated outline of the subject; readable.

*A History of Medicine* by Douglas Guthrie. London, Nelson, 1945.

*A History of Medicine* by Ralph H. Major. 2 vols. Oxford, Blackwell, 1954. Profusely and excellently illustrated.

*Eternal Eve* by Harvey Graham. London, Heinemann, 1950. This book deals mainly with obstetrics, but it contains much of general interest. Not always accurate, it suffers from lack of references, but it is well worth reading.

Of books dealing specifically with the history of anaesthesia, the most important are:

*The Development of Inhalation Anaesthesia* by Barbara M. Duncum. London, Oxford University Press, 1947. This is an outstanding book, accurate, comprehensive, well illustrated and fully documented.

*The History of Surgical Anesthesia* by Thomas E. Keys. New York, Schuman, 1945. Another valuable book; it contains a most useful chronology of events and many important references.

*Ancient Anodynes* by E. S. Ellis. London, Heinemann, 1946. This is a useful compilation of incidents and events, mostly in note form, with many references.

*The English Pioneers of Anaesthesia* by F. F. Cartwright. Bristol, Wright, 1952. Deals in great detail with Priestley, Davy, and Hickman, and thus covers the "pre-anaesthetic" period. Very fully documented.

*Triumph over Pain* by R. Fülöp-Miller, translated by E. and C. Paul. New York, Bobbs-Merrill, 1938. A "romantic" book, without references, frequently inaccurate in details, it is nevertheless an interpretation of the history of anaesthesia which makes enjoyable reading.

In addition, there are numerous biographies of people such as Sir James Y. Simpson, Sir Benjamin W. Richardson, Joseph Priestley, John Snow, and Crawford W. Long, which can be studied with profit. Special articles are also to be found in the *British Journal of Anaesthesia* (commenced publication 1924), *Current Researches in Anesthesia and Analgesia* (commenced publication 1922), *Anaesthesia* (commenced publication 1946), and in the *Proceedings of the Royal Society of Medicine*. The issue of the *Journal of the History of Medicine and Allied Sciences* (Vol. I, No. 4) for October 1946, was a special "Anaesthesia Centennial Number" and contains a great deal of important material.

As a general rule the "potted" history given in chapters on this subject in anaesthetic textbooks is of little value, but exception may be made in the cases of *A Synopsis of Anaesthesia* by J. Alfred Lee, Bristol, Wright, 3rd edition, 1953, whose chronology is helpful and down to earth, and *Essentials of General Anaesthesia* by Sir Robert Macintosh and Freda K. Bannister, Oxford, Blackwell, 5th edition, 1952, which is accurate and entertaining. For the history of endotracheal and allied methods, *Endotracheal Anaesthesia* by Noel Gillespie, University of

Wisconsin Press, 2nd edition, 1948, and *The Principles of Thoracic Anaesthesia, Past and Present* by William W. Mushin and L. Rendell-Baker, Oxford, Blackwell, 1953, are particularly informative and well illustrated.

### CHRONOLOGY OF THE HISTORY OF ANAESTHESIA

For our purpose, the main stream of history can be divided into certain fairly well-defined periods:

A. Pre-historic, up to about 3000 B.C. (Nile Valley, Mesopotamia).
B. Magico-Empiric, 3000–585 B.C. (Nile Valley, Mesopotamia).
C. Scientific, 585 B.C.–200 A.D. (Asia Minor, Greece, Alexandria, Rome).
D. Superstitious, 200–1454 A.D. (Constantinople, Arabia, Western Europe).
E. Renaissance, 1454–1754 A.D. (Western Europe).
F. Pre-anaesthetic, 1754–1846 A.D. (Western Europe and America).
G. Anaesthetic, 1846 onwards.

### A. *Prehistoric Age* (*until c.* 3000 B.C.)

The prehistoric races which settled in the Nile Valley and the Mesopotamian region were similar to such races in other parts of the world. They passed through the usual neolithic and chalcolithic stages of development. In the absence of written records, direct evidence can only be obtained from archaeological discoveries, particularly of interments. Indirect evidence is available by the examination of the customs of recent and present-day primitive peoples whose culture has reached a similar stage of development but such evidence must, of course, be treated with caution.

The cause of disease is ascribed by such peoples to the wrath of a god or gods, who either make use of material objects to injure the people who have insulted them, or else fire magical "elfshot" into them. Sometimes a demon or spirit may take up his abode within a man, and thus cause disease, physical or mental. By means of magic, some men may be able to make the spirits to do their bidding, and thus disease may be caused by a "powerful" enemy.

The treatment of disease, therefore, consists of placating the wrathful god by means of magical rites, removing the magic "elfshot" or, if the patient be inhabited by a spirit, making him so uncomfortable that the spirit will be glad to go elsewhere. The need for special knowledge and powers to carry out the magical rites correctly led to the establishment of the witch-doctor. When medicines were administered to the patient for the purpose of driving out a spirit, they were usually unpleasant and revolting by nature, frequently compounded of various sorts of animal and human excreta; evil-smelling herbs were also employed, and perhaps plants with specific but drastic action, such as castor oil seeds, while other herbs were employed for purely magical reasons. There was no trace of rational medicine; the administration of substances to produce a specific pharmacological action was unthinkable.

Surgery existed at three levels. First, a crude knowledge of anatomy was helpful in killing and preparing animals for food. Secondly, wounds received in battle or the chase were obviously bandaged and given some sort of first aid. Thirdly, ritual operations were carried out. As the latter were, to some extent at least, tests of endurance and evidence of manhood, anaesthesia was undesirable.

In many parts of the world, trephined skulls are found dating back to neolithic times. It has been suggested that this was done for the treatment of headache; it seems more probable that it was for the evacuation of an obstinate demon, who might manifest his presence in many other ways, such as madness or delirium, or it may have been a purely magical rite: the removed discs of bone were often used as amulets. No such skulls have been discovered in the Nile Valley or in Mesopotamia.

The inevitable conclusion is that, in the prehistoric era, there was no knowledge of pain-allaying drugs; the rational basis of pharmacology was entirely lacking, and medicine was purely magical in nature.

### B. *The Magico-Empiric Age* (*c.* 3000–585 B.C.)

Sometime about the end of the fourth millennium B.C., the great civilizations of the Nile Valley and of Mesopotamia came into existence. While there are many points of resemblance between these two cultures, there was one important difference: in Mesopotamia there was constant

rivalry between city states, now one and now another being dominant, while in the Nile Valley the government was centralized, the whole of Egypt being under one authority, save for comparatively short periods.

The major part of our knowledge of Egyptian medicine is derived from a number of papyri, most important of which is the Ebers Papyrus, which was written in the XVIIIth Dynasty (about 1500 B.C.) but was undoubtedly copied from much older sources. From this alone we are able to form a good idea of the state of Egyptian medical knowledge, while the other papyri, earlier and later, substantiate our ideas. The continuance of a central government, coupled with Egyptian reverence for the past, led to a relatively static state of culture, and, during the period under consideration, medicine changed but little. Egypt attained a high level of culture early in her history, but she failed to show great advances afterwards.

Egyptian medicine was compounded of two elements: magic and rational methods. The action of some drugs (e.g. the diuresis caused by juniper berries) was known, but magical rites were always performed with the administration of drugs, and often drugs were omitted, treatment being by magic alone. Diseases were still personified, and thought to be due to the presence of a god or goddess in the patient. Surgery seems to have been limited to circumcision and to the first-aid treatment of wounds and fractures. The use of "plaster" casts, made of gums and so forth, for the treatment of fractures was highly rational.

The knowledge of anatomy was very limited: the same word was used for veins, arteries, nerves, and muscles. There was, however, some idea of the gross details of the larger viscera, since these were removed in the process of embalming. As, however, the men who were employed to do the evisceration of corpses were considered to be polluted and outcast, the influence of embalming on anatomical knowledge was very slight.

The Egyptians used many drugs: unfortunately, only a few of them can be identified. There is no evidence that they used any anaesthetic or pain-allaying drugs, and such carvings and frescoes as depict surgical operations always indicate a fully conscious patient.

The Mesopotamian cultures developed a system of medicine that was very similar to that of Egypt. Diseases were caused by demons, special demons being responsible for definite diseases, some degree of diagnosis being made, e.g. "wasting disease", "liver disease". Apparently, the physicians were priests. Surgery seems to have been in the hands of craftsmen: in the Code of Khammurabi (about 1700 B.C.) the rewards for successful, and punishments for unsuccessful, operations are laid down, but no attempt is made to regulate the activities of physicians.

The Mesopotamian list of drugs is large and, as in Egypt, some of them had therapeutic properties. Some crude knowledge of anatomy existed, fostered, no doubt, by the custom of divination from the entrails, especially the liver, of animals. Medicine marched hand in hand with magic, and what rational treatment was adopted was purely empiric. There is no evidence that anaesthetics were attempted or that pain-relieving drugs were known. Some authorities claim that the Assyrians were familiar with mandragora, a Greek word which they derive from Assyrian nam-ta-ira. The argument is unconvincing.

According to Hoffman (*De Thorace*, 1625) the Assyrians were accustomed to compress the vessels in the neck in order to produce insensibility during the operation of circumcision. In the seventeenth century, knowledge of Assyria was scant, and the Assyrian language was undecipherable. Hoffman's remark has been copied by subsequent authors, but may safely be disregarded as without foundation.

Astronomical observations were made and recorded with great assiduity by the Mesopotamians, who developed a system of counting based on the unit 60. This is the origin of our subdivisions of the hour (60 minutes each of 60 seconds) and of the circle (360 degrees each of 60 minutes, each minute being 60 seconds). Both at the time of the French Revolution and of the Nazi hegemony, attempts were made to subdivide the circle into 400 degrees, but the hand of Sumer was not to be wrested from astronomical studies.

The Hebrew culture sprang to life in Palestine, under the influence of both Egypt and Mesopotamia. In medicine, the Hebrews made great advances in hygiene, but surgery and therapeutics remained respectively primitive and superstitious.

Anaesthesia was unknown, although, at a later date, mandrakes seem to have been credited with magical properties. The great contribution which they gave to the world was, of course, monotheism.

It must be realized that the dates given in the chronology below are not final. Archaeologists frequently revise their schemes of dates, and the older the period, the greater the chance of error. The dates here given are usually in accord with Albright (*Bulletin of the American Schools of Oriental Research*, 1942, 88, 32).

B.C.

*c.* 2900. Old Egyptian Kingdom: 1st Dynasty begins with King Menes.

*c.* 2800. After the great flood in the Mesopotamian region, relics of which were discovered at Ur, the early Sumerian Dynastic Period begins.

*c.* 2700. Tjeser (Zoser), first King of the Egyptian IIIrd Dynasty. His "vizier' was the Priest-Physician, Imhotep, who designed, it is believed, the first pyramid (the step-pyramid at Saqqara). Imhotep is probably the first physician whose name has come down to us; his memory was greatly revered in after ages, and, by the end of the Magico-Empiric Age, he had received his apotheosis as God of Healing.

*c.* 2600. The Great Pyramid of Egypt built by King Khufu.

*c.* 2360. Sargon of Akkad becomes master of Babylonia.

*c.* 2250 (?). Cunciform tablets from Nippur (Babylonia) have been found which describe the treatment of dental decay by the local application of a gum containing, among other things, seeds of henbane. It is perhaps stretching a point to call this "the earliest record of local anaesthesia" (Major, op. cit.). The date of these tablets is probably considerably later than cited.

*c.* 2200–1989. Intermediate period of collapse of central government in Egypt (VIIth–XIth Dynasties).

*c.* 2180. Babylonia overrun by the Gutians (King Gudea).

*c.* 1989–1776. The Middle Kingdom of Egypt.

*c.* 1960–1830. Elamite and Amorite invasions of Babylonia.

*c.* 1935. The migration of Abraham from Ur (anachronistically called "of the Chaldees" in the Bible) may have occurred at about this time.

*c.* 1830. The Old Babylonian Period begins.

*c.* 1776–1570. Intermediate period of collapse of central government in Egypt. It was during this period that the Hyksos ("foreign kings") made themselves masters of Egypt. Some have identified the Hyksos with the Israelites, but this identification is certainly wrong. They seem to have come originally from Asia Minor.

B.C.

*c.* 1748–1716. Shamshi-Adad I, King of Assyria.

*c.* 1728–1676. Khammurabi, King of Babylonia. The name "Habiru" (Hebrews?) begins to appear in Mesopotamian inscriptions.

A black diorite stela, some 6 feet tall, inscribed with the Code of Khammurabi, has been discovered at Susa, whither it had been taken by the Elamites. It is headed with a relief of Khammurabi receiving the Law from the Sun-God. Underneath are nearly 300 paragraphs, some of which refer to the duties, fees and responsibilities of surgeons. It is difficult to believe that the brutal punishments awarded to unsuccessful practitioners can have been intended to be inflicted in ordinary cases. For instance, if the opening of an abscess in the eye was followed by loss of sight, the surgeon's fingers were to be cut off. There is no evidence of any form of anaesthesia, and physicians are not discussed.

*c.* 1570–1150. The New Empire of Egypt. Aames, the first King of the XVIIIth Dynasty. Thothmes the Great extends Egyptian rule to the Euphrates.

It is to the earlier part of this period that the Ebers papyrus is to be assigned, although it was undoubtedly copied from books of a much earlier date. It consists of a list of prescriptions for various diseases, which are named, but no assistance towards diagnosis is given. There are many magical rites. It seems to have been a "Handy Home Doctor", rather than a physician's text.

Other medical papyri have also been discovered: the Ramesseum Papyri (XIIth Dynasty); the Kahûn Papyrus, mainly gynaecological, of about the same date; the Hearst, the Edwin Smith, the London (all XVIIIth Dynasty); the Berlin (XIXth Dynasty), and the nineteen Chester-Beatty Papyri (XXth Dynasty). All show a strong predilection for magic. No mention is made of anaesthesia or opiates, but it must be borne in mind that translation is often difficult or impossible. "Didi", at first translated "Mandrake", is now known to have been a mineral (haematite).

*c.* 1400. The Exodus is usually dated at about this time.

*c.* 1377. Accession of Amenhotep IV (the "Heretic King" Akhnaten) to the throne of Egypt. Subbilluliuma, King of the Hittites. Ashur-uballit I, King of Assyria.

It was during the reigns of Amenhotep IV and his father that the collection of "Tell-el-Amarna" letters was made. The Egyptian empire was threatened, and, among others, the Habiru were attacking Palestine from the East.

Tutankhamen, originally called Tutankhaten, succeeded Akhnaten after a short interval. An attempt has been made to identify him with the Pharoah of the Exodus, but this is unlikely. Unfortunately, Egyptian records are completely silent about the presence of the Children of Israel in Egypt.

B.C.

*c.* 1301–1234. Rameses II (the Great), XIXth Dynasty. The empire maintained by constant fighting. The Temple of Karnak, which dwarfs St. Peter's at Rome, and many other colossal building projects undertaken.

*c.* 1250 The Children of Israel come into the Promised Land. (Palestinian Early Iron Age).

*c.* 1150. The Decline of Egyptian power (XXIst Dynasty). The Siege of Troy may be assigned to this period.

*c.* 1000. David, King in Israel, makes Jerusalem his capital.

*c.* 950. Solomon builds the temple in Jerusalem.

*c.* 950–900. The Homeric period. Although the Odyssey was not written down until a much later period, the poem probably altered little. The herb Moly, perhaps the earliest ancestor of the Mandrake, is mentioned in the tenth Book. Kirke has turned Odysseus' men into swine. He sets forth to rescue them and is met by the god Hermes, who offers him the herb, whereby he may overcome the magic of Kirke. The plant is described with some minuteness. " It was black at the root, but the flower was like to milk. ' Moly ' the gods call it, but it is hard for mortal man to dig, howbeit, with the gods, all things are possible ".

883–859. Ashur-nasir-pal II makes Assyria an armed camp. He began the reign of terror which made the cruelty of the Assyrians a byword.

B.C.

874. The foundation of Carthage.

776. Greek chronology begins with the first Olympiad.

753. Roman chronology begins with the foundation of the city of Rome.

744–727. Tiglath-Pileser III, King of Assyria and conqueror of Babylonia, over-runs Palestine and deports many of the Israelites.

704–681. Sennacherib, King of Assyria. He besieges Jerusalem, but raises the seige, perhaps on account of plague.

*c.* 700. Isaiah, the prophet.

669–633. Ashurbanipal, King of Assyria. He gathered a huge library, many of the " books " being copies of older texts, some very old. There are some 800 medical prescriptions including one for toothache (cf. *c.*2250 B.C. above), a local application containing, among other things, mustard! The prescriptions are largely magical, and contain many incantations.

*c.* 624–565. Thales of Miletus, founder of Greek science.

612. Fall of the Assyrian empire. Nineveh destroyed by the Medes and Persians.

594. Solon codifies Athenian law.

587. Destruction of Jerusalem by Nebuchadnezzar II of Babylon.

539. Babylon falls to Cyrus the Persian. The end of the " Babylonian Captivity ".

*(To be continued)*

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## CORRESPONDENCE

### BRONCHIAL TUBE AND BLOCKER

Sir.—In their observations under this heading in your May issue your correspondents, referring to the article by Dr. Leatherdale and myself (*Brit. J. Anaesth.* (1955), **27**, 556), state that the indications for one lung anaesthesia " will always continue "—and then give the reasons why they advocate the insertion of endobronchial tube or blocker under direct vision, through a bronchoscope. This conventional method presents little difficulty to my co-author, Dr. Leatherdale, since he has had the undisputed advantage of being trained by a colleague well versed in the art. To me, however, and to hundreds of others who have not enjoyed the privilege of such training, the *accurate* location, through a bronchoscope, of endobronchial tube or blocker is no easy matter: moreover the tubes and blockers used in this procedure are readily dislodged.

We wouldn't presume to suggest to experts how they should tackle the sort of job they meet every day. When we published the description of the tube and blocker which can be passed blindly we had in mind the predicament of the anaesthetist called on to work in a field in which he is not thoroughly at home. I still believe that anaesthetists in this category will intubate or block a bronchus more accurately, and with less disturbance to the patient, by the blind method we describe and, what is more, these shaped tubes and blockers are less likely to become displaced.

It is a reasonable assumption that a patient on whom one lung anaesthesia is contemplated will have been examined through a standard bronchoscope shortly before operation. This investigation is well within the province of a trained anaesthetist. The art of using the specially

[*Continued on page 287*

*Brit. J. Anaesth.* (1956), **28**, 284

# ATTRACTING THE UNDERGRADUATE

BY

R. BRYCE-SMITH*

*Nuffield Department of Anaesthetics, University of Oxford*

A FEW years ago, one of the first duties that might be required of a newly qualified practitioner was the administration of general anaesthetics. Today, it is more than likely that his successor may give the only anaesthetics of his career as a medical student under supervision. The National Health Service has virtually banished the occasional anaesthetist and the general practitioner who always gave anaesthetics to his own patients for surgical procedures. The opportunities for the general practitioner to practise anaesthesia are now limited almost entirely to the dental "gas" or to the field of obstetrics. This is a paradoxical situation since it is recognized that both are potentially hazardous and present difficulties even to the most highly skilled. This is not a criticism of the general practitioner but rather of the circumstances which place him in such an invidious position.

This, then, is the situation. Hospitals are now staffed with full-time anaesthetists (in varying stages of training it is agreed), and allow no opportunities for the nonanaesthetic house officer; while to the general practitioner, bereft of all anaesthetic experience, is left one of the most difficult and dangerous of all tasks. This is the background against which the medical student receives his training in anaesthetics.

It would seem that before discussing the ways by which recruits may be attracted to anaesthesia, it is necessary to decide what the student must be taught about anaesthetics. Also, and equally important, when the medical curriculum is already so full, what object there is in view in teaching him the subject at all. No clear answer can be given to either, but the time has surely come to review the position and possibly revise our plans for the future. Before attempting to find solutions to these problems, our own minds should be clear on a number of points:

(1) Should anaesthetics be given only by qualified anaesthetists? In answering this the matter must be brought down to a personal level and we must consider whether we are willing to allow our families or ourselves to be anaesthetized by a nonspecialist.

(2) Is it advisable to give every house officer opportunities (if there is time) to gain experience in anaesthesia?

(3) Is it reasonable to expect the general practitioner to administer anaesthetics for childbirth only—is it fair to the mother or the doctor?

If we accept the fact that all qualified practitioners should be capable of administering an anaesthetic, it is not easy to know what anaesthetic techniques they should be taught. Above all, these techniques must be safe and must be applicable on a variety of occasions including domiciliary obstetrics. There is a moral, and unhappily there may be a legal issue at stake. But even if these two interests are identical, it is more than likely that the local and not the ideal circumstances will provide the answer.

One solution lies in the expansion of our anaesthetic services, so that there will never be either the excuse or the need for anyone other than a specialist to give an anaesthetic in any form of practice. If this is the solution, then many recruits are needed, and these should be the pick of the students and not the "cast-offs" from every other branch of medicine. If quality is sacrificed for quantity, the specialty will fall into disrepute and the status of which we are so proud will be no better than in those countries where the anaesthetic specialist is unknown. But everybody wants the

* The opinions expressed in this article are those of the author only and do not necessarily represent the views of the Nuffield Department of Anaesthetics.

best. If we are to have it, then strenuous efforts must be made to make the specialty more attractive *as early as possible* in the student's course of training. The undergraduate must be caught before he can be seduced by the more glamorous enticements of other specialist branches.

Under the scheme of teaching at most centres, this is not possible, for instruction in anaesthetics is usually encountered shortly before qualification. By that time, the student has been subjected to the influences of almost every other department and his future interests are almost decided—at least for the time being. The arguments advanced in favour of this course of events claim that an essentially practical subject, for which so little time is available, is likely to remain fresh in the mind and therefore ready for instant application if it is taught as nearly as possible to the time when it is to be used. With the preregistration year ahead, this is no longer true.

During the last few years, students at Oxford have received their courses in anaesthetics soon after entering hospital during their first surgical term. This procedure was adopted with reluctance in order to fit in with an amended curriculum. To our surprise, the results of this change have been most gratifying and two points have emerged:

(1) The students appear to take a greater and more intelligent interest in the lectures, presumably because they are not yet saturated with medical facts.

(2) They have shown an increased keeness during their course of practical instruction. This has been shown by much spare time spent in waiting and hoping for emergency patients, and by the total number of anaesthetics administered. In many instances, this has amounted to almost double the number performed under the former régime.

It is suggested that these results confirm the opinion that an early approach to the student is well worth while. Without in any way altering the syllabus or opportunities except in the time relationship to the rest of the clinical course, anaesthesia is arousing more interest. This is probably because the administration of anaesthetics now offers one of the earliest occasions for doing some " practical doctoring " and accepting some small measure of responsibility. At this early and impressionable stage in his career, the student has not had time to become blasé and is grateful for any clinical crumbs that may be thrown to him. Two weeks of activity devoted to giving anaesthetics is a very large crumb, and although this period will have little influence on his future ability as an anaesthetist, it may whet his appetite for further knowledge. At least, it gives us an opportunity to present a few aspects of our specialty to a receptive mind.

It is too early to claim that the early presentation of anaesthetics to the students will provide, *ipso facto*, a constant stream of would-be anaesthetists, but already several have expressed an interest in adopting anaesthesia as a career. This in itself is an advance, and most welcome after a series of sterile courses when the members' one aim in life has been to get " signed up " as painlessly as possible and have done with yet another infliction deemed necessary by the authorities.

But if an early approach to the student has any virtue, why wait until the clinical years? During the pharmacology course drugs used by the anaesthetist are considered alongside aperients, antibiotics and anthelmintics, and capital can be made out of this fact. Such an idea is not original, for the opportunity has been already recognized by many medical schools in the United States where the manpower shortage in anaesthesia is far worse than in the United Kingdom. In Cleveland, Ohio, at Western Reserve University, sixteen hours of pharmacology lectures are now devoted to anaesthesia, and are undertaken by members of the Department of Anaesthetics. This is in no sense a criticism of the ability of the pharmacologists, but may be regarded as a veritable monument of cooperation and goodwill between two departments. In this course, more time is devoted to demonstrations than to lectures, and with the emphasis on the practical application of anaesthetic drugs rather than their pharmacological properties. It is for this reason that the anaesthetist takes over from the pharmacologist. The result may not be an epitome of didactic teaching, but it demonstrates very vividly the potentialities, and not infrequently, the unrehearsed dangers of anaesthesia.

The purist would undoubtedly describe the performance of spinal and caudal blocks on dogs, and

rabbits subjected to open ether to show the stages of anaesthesia, and of cats brought to cardiac arrest with chloroform, as mere window dressing. So indeed it is, and achieved only at the expense of much time on the part of the anaesthetists.

But the results have justified the experiment, and at this particular school, it is the surgeons who now have a shortage of recruits owing to the transferred loyalties of several prospective residents. This is demonstrated in another and more positive way by an increase in the number of anaesthetic residents from one to twelve during the past five years. This change has been brought about by many factors of which a deliberate expansion policy has been the most important, but there is no doubt that the efforts made during the pharmacology course have played a part, if merely by arousing interest in a hitherto colourless and disregarded subject.

Respiratory physiology presents another opportunity during the preclinical years in which the problems of the anaesthetist may be brought to light. Yet most physiology courses never mention the word anaesthesia, although the importance of an efficient respiratory exchange, with all that this entails, is well recognized by every candidate for the D.A. and F.F.A. The establishment of respiratory units up and down the country has stressed the necessity for a proper understanding of the treatment of respiratory failure, and these units could serve as ideal examples for the practical application of what are all too often academic facts. Also, but by no means less important, this linkage could show that the scope of anaesthesia is extending beyond the confines of the operating theatre. An early introduction, and active participation in the administration of anaesthetics as soon as possible, should therefore be the two major aims in any programme designed to attract the undergraduate.

Next, a departure from the usual reserved attitude of many senior anaesthetists towards students' activities is desirable. This may be regarded as a poor substitute for the regular and

frequent contacts of ward rounds and clinics which provide the common meeting ground for other members of the hospital staff. In other words, opportunites must be made for students and anaesthetists to get to know each other and, it may be hoped, to develop a mutual respect.

If these efforts are successful, yet another problem remains: how to maintain and foster this interest for possibly two more years before the recruit is ready to join a Department of Anaesthetics. Somehow, the activities of the department must be brought to his notice. Open invitations to attend meetings are obvious, but are unlikely to attract much attention—the student knows all too well that most of the discussions will be too technical and far above his head. A possible alternative lies in the establishment, with the approval and support of the medical school, of monthly or even quarterly seminars. These should be given by members of the Anaesthetic Department, but designed for a nonanaesthetic audience. The subject matter must, therefore, be of general interest but with a strong anaesthetic flavour.

If these suggestions are put into effect, it is well to realize that they entail much hard work by the anaesthetists. Care and forethought must go into every lecture and demonstration so that the final result becomes a polished performance. A slapdash approach will be calamitous and do more harm than good. The intention throughout must be to present anaesthesia as a specialty worthy of being adopted as a career. For those who have other loyalties, this programme will at least give them an opportunity to appreciate the problems of anaesthesia and enable them to explain to patients what may be expected at an impending operation. For this last reason alone, it is obvious that instruction in anaesthesia is an essential part of the medical curriculum. But with the high standards of safety demanded today, it is not possible to train a practising anaesthetist in two short weeks. Such a concept must be forgotten and it must be realized that the man who is going to administer anaesthetics, under any circumstances, should have postgraduate training.

A system designed to attract the undergraduate must rely finally on the anaesthetists themselves, the example they set in their work, the interest they show in student teaching, and the help they are prepared to give in developing the ever widening field of anaesthesia. The fact that advertisements have an unselective appeal must be accepted, but the high standards of the F.F.A. can be relied on to select the best with impartial, if not loving, care.

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CORRESPONDENCE (*continued from page* 283)

designed small Magill bronchoscope, on which the bronchial tube is carried, is quite another matter, and is acquired only after considerable experience.

We are commended for incorporating in the proximal part of the endobronchial tube a small catheter to aspirate secretions from the lung put out of action. I would repeat that this catheter has been found useful too, to distend the nonfunctioning lung with oxygen, at the surgeon's request, to facilitate dissection.

It is a tribute to the demands made on the space of your monthly Journal that our article and the comments on it are separated by the space of six months. I would be sorry, however, if after this interval the reader did not have the original article to hand to judge whether the wording of one of the comments is justified. Sturtzbecher did not describe an endobronchial tube. His blocker was the first to be attached to an endotracheal tube, and it was for this reason that we inserted his name (in brackets) immediately after the heading "*Endobronchial blocker*". We also added the names of Mülly and Hossli because they gave an excellent description and diagrams of Sturtzbecher's blocker. And at the end of our article these authors constitute two of the three references.

R. R. MACINTOSH
*Pembroke College, Oxford*

*Brit. J. Anaesth.* (1956), **28**, 288

# VISUAL AIDS IN THE UNDERGRADUATE TEACHING OF ANAESTHESIA

BY

A. H. GALLEY

*King's College Hospital, London*

BOOKS and diagrams are no substitute for personal training in any practical subject—particularly that of the administration of anaesthetics to human beings where faulty technique may lead to temporary or permanent disabilities or even death. Even in this subject, however, visual aids may be useful to the teacher and his student; they help to maintain a logical sequence of instruction and reinforce the auditory stimuli associated with personal teaching.

The good teacher should emulate the example of Euclid and proceed from the known to the unknown—thereafter using each newly found piece of knowledge as the launching site for further flights into the realm of the unknown. These charts have been designed to enable this to be accomplished when teaching the art and science of anaesthesia.

## FACTORS AFFECTING THE RESPIRATORY CENTRE DURING ANAESTHESIA

In figure 1 the student is reminded of certain aspects of the physiology and pharmacology associated with the respiratory centre; here they are correlated from the point of view of the anaesthetist. This triple chart enables one to demon-

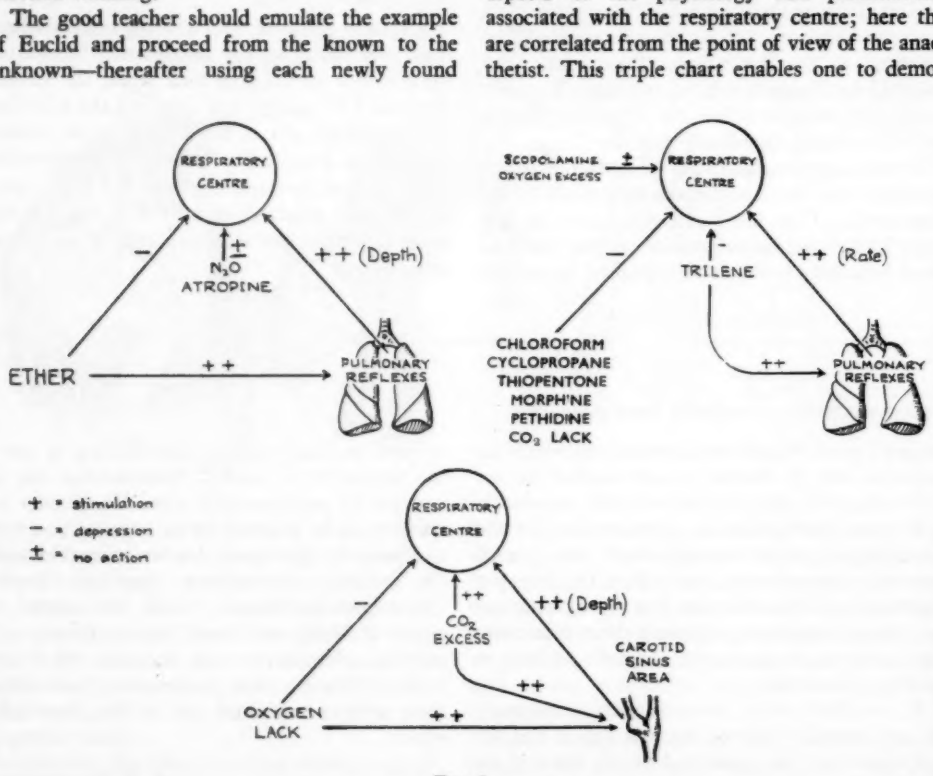



FIG. 1

Factors affecting the respiratory centre during anaesthesia.

strate that oxygen and carbon dioxide lack and carbon dioxide excess have just as potent an influence upon the behaviour of the respiratory centre as the drugs employed during anaesthesia. Elementary facts, therefore, such as the value and necessity of maintaining a patent airway can be stressed equally with the dangers of administering an overdose of anaesthetic. In addition, the contrasting manner in which ethyl ether and trichlorethylene "stimulate" the respiratory centre can be elucidated if required.

### COMPONENTS

Figure 2 demonstrates the now well-known conception that anaesthesia is a mixture of hypnosis, analgesia and muscular relaxation.

In figures 3 and 4 "analgesia" is depicted as being composed of "touch" and "pain", in order later to differentiate some of the side effects of general and local analgetics (analgesics). "Relaxation of Muscles" is subdivided into three

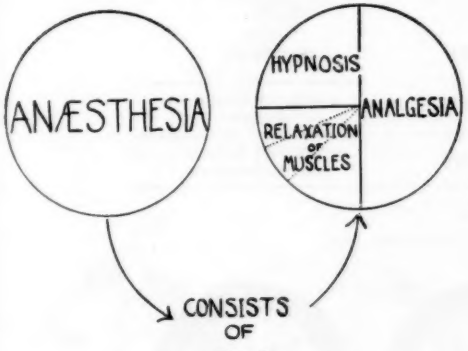



FIG. 2
Components of Anaesthesia.

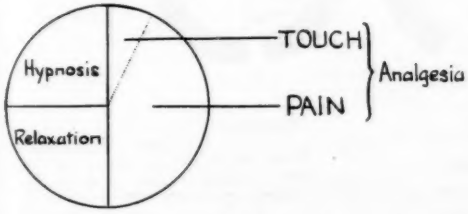



FIG. 3
Components of analgesia during anaesthesia.

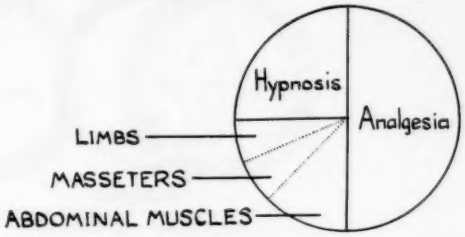



FIG. 4
Components of "muscular relaxation" during anaesthesia.

lesser components: "limbs", "masseters" and "abdominal muscles". This triple subdivision enables the instructor to differentiate between those anaesthetics which readily relax the jaw muscles and those which do not; those which allow manipulations of the limbs to be carried out under light anaesthesia; and the tricks to which the anaesthetist resorts to obtain abdominal muscle relaxation at those lighter planes of surgical anaesthesia which are unaccompanied by "anaesthetic shock", i.e. circulatory depression due to depth of anaesthesia per se (Galley, 1949).

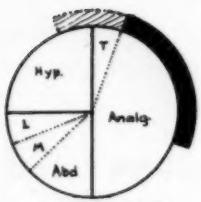
### ANAESTHETIC COVER

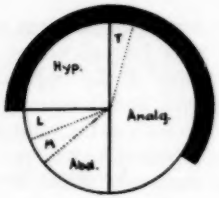
There are thirteen charts (figs. 5–17) which demonstrate anaesthetic cover by a thick black line external to the circle containing the components of anaesthesia. The disposition of the "components" has been so arranged that in most cases the black line at the periphery is undivided but, in the case of local and spinal analgesia, the line is interrupted. Each chart demonstrates two or more examples so that, either the variation of cover at different depths of anaesthesia is indicated or the effect produced by adding additional drugs to a basic mixture.

At the base of each chart is a simple explanation of how respiration and the circulation are affected. In other words, the upper part of the chart shows the cover given and the lower portion the price we have to pay!

### GENERAL NOTE

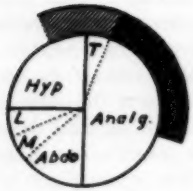
Truth is usually far too complex to be contained by the proverbial nutshell. Oversimplifica-

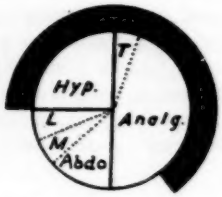



| | "Analgesia" | Anaesthesia |
|---|---|---|
| Respiration | Unaffected | Slightly stimulated |
| Circulation | Unaffected | Slightly stimulated |

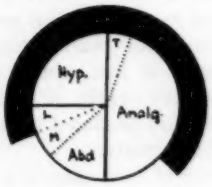
FIG. 5
Anaesthetic cover 1: Nitrous oxide

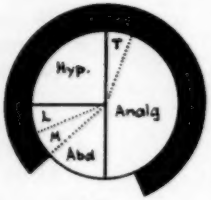


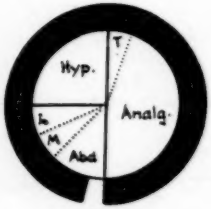



| | "Analgesia" | Light anaesthesia | Deep anaesthesia |
|---|---|---|---|
| Respiration | Hastened | Rapid | Very rapid and shallow |
| Circulation | Unaffected | Unaffected | Gradual failure due to hypoxia |

FIG. 6
Anaesthetic cover 2: Trichlorethylene

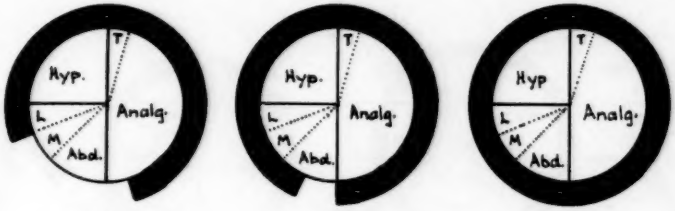


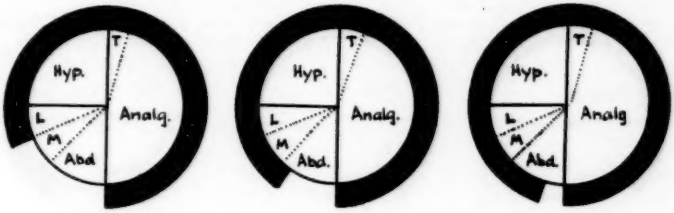

| | Light | Surgical | Deep |
|---|---|---|---|
| Respiration | Stimulated | Normal | Depressed |
| Circulation | Stimulated | Stimulated | Slow but steady deterioration |

FIG. 7
Anaesthetic cover 3: Ether



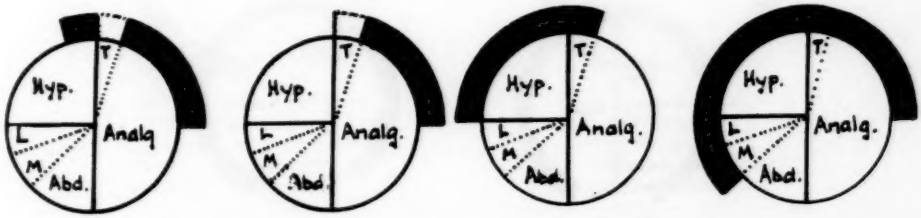

| | Light | Surgical | Deep |
|---|---|---|---|
| Respiration | Depressed | Depressed | Rapid collapse |
| Circulation | Depressed | Depressed | |

FIG. 8
Anaesthetic cover 4: Chloroform



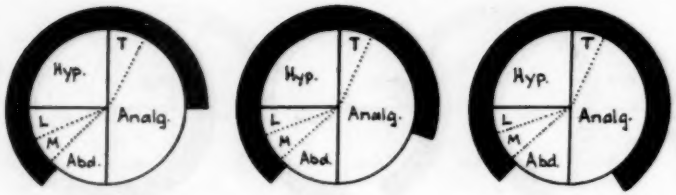

| | Light | Surgical | Deep |
|---|---|---|---|
| Respiration | Depressed | Depressed | Apnoea—But circulation intact if artificial respiration is instituted (pulse may be irregular) |
| Circulation | Stimulated | Stimulated | |

FIG. 9
Anaesthetic cover 5: Cyclopropane



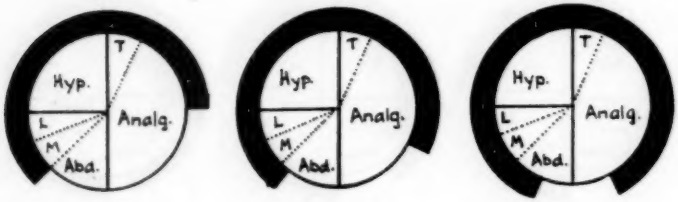

| | Morphia | Pethidine (Syn: Demerol.) | Pentobarbitone | Light thiopentone (Syn: Intraval or Pentothal) |
|---|---|---|---|---|
| Respirations | Depressed+ | Depressed+ | Depressed+ | Depressed+ to ++ |
| Circulation | Unaffected | Unaffected | Depressed | Depressed+ |

FIG. 10
Anaesthetic cover 6



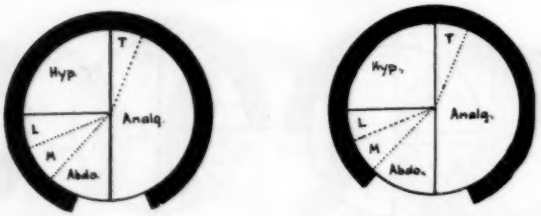

| | Light | Surgical | Deep |
|---|---|---|---|
| Respiration | Depressed | Depression or apnoea but the circulation remains intact if respirations are "assisted" | Reversible or irreversible failure |
| Circulation | Unaffected | | Collapse |

FIG. 11
Anaesthetic cover 7: Thiopentone



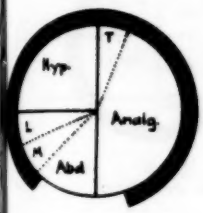

| | Thiopentone (light) | Ditto plus morphine | Ditto plus nitrous oxide |
|---|---|---|---|
| Respiration | Depressed | Depressed | Depressed |
| Circulation | Unaffected | Unaffected | Unaffected |

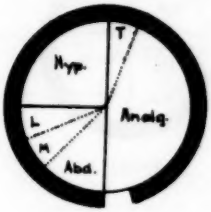
FIG. 12
Anaesthetic cover 8: Thiopentone-Morphine-$N_2O$




| | Deep thiopentone | Light thiopentone Plus morphine and $N_2O$ |
|---|---|---|
| Respirations | Reversible or irreversible failure | Depressed or apnoea |
| Circulation | Collapse | Unaffected if "assisted" or artificial respiration is effective. |

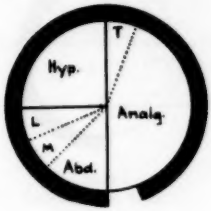
FIG. 13
Anaesthetic cover 9

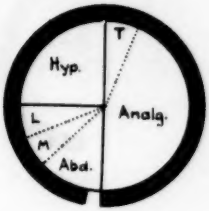



| | Morphine, thiopentone and nitrous oxide | Ditto—plus curare or curare substitute |
|---|---|---|
| Respiration | Depressed | Depressed or apnoea |
| Circulation | Unaffected | Unaffected if "assisted" or artificial respiration is employed. |

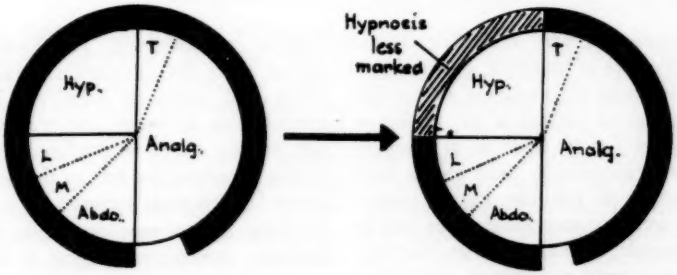
FIG. 14
Anaesthetic cover 10




| | Light thiopentone anaesthesia plus morphine, curare and $N_2O$ | Deep ether anaesthesia |
|---|---|---|
| Respiration | Depressed or apnoea | Very depressed |
| Circulation | Unaffected if "assisted" or artificial respiration is employed. | Circulation steadily deteriorates. |

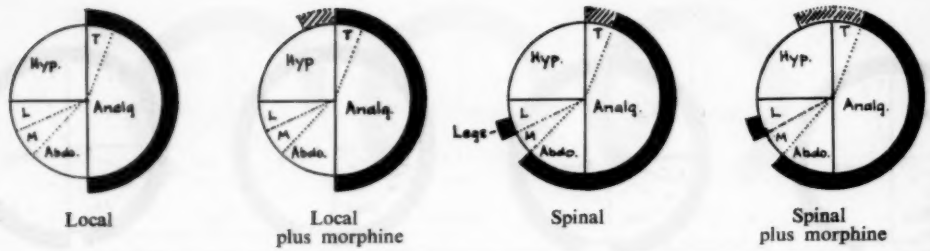
FIG. 15
Anaesthetic cover 11



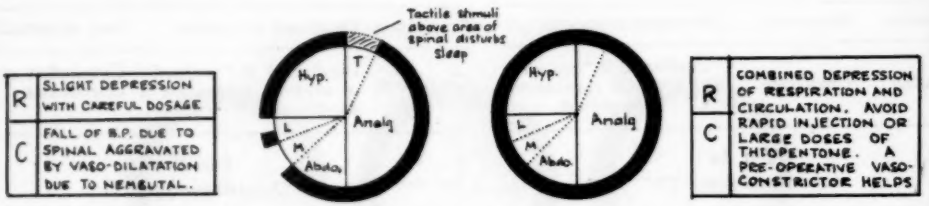

INDUCTION — MAINTENANCE

| | Morphine, thiopentone curare and nitrous oxide | Pethidine, curare and nitrous oxide |
|---|---|---|
| Respiration | Depth diminished or apnoea | Rate diminished or apnoea |
| Circulation | Intact if lung ventilation efficient | Intact if lung ventilation effective |
| Recovery | Fairly slow | Rapid with absence of pain |

FIG. 16
Anaesthetic cover 12




| | | | | |
|---|---|---|---|---|
| Respiration | Intact | Slightly depressed | Depression increases with height of spinal | Depression increases with height of spinal |
| Circulation | Intact | Intact | | |




N.B.—All spinals should be given oxygen.

FIG. 17
Anaesthetic cover 13: Locals and spinals

tion can, by omission, be very misleading. However, as in all branches of teaching, complexities are usually omitted from early training so that the student can visualize an outline of his subject—the details of which can be filled in as comprehension increases. Accordingly, these charts have been kept as simple as possible; but to enable this to be done certain compromises have had to be made. For example, no differentiation has been made between peripheral and central circulatory failure—this has been left to the teacher to add if and when he thinks fit. Nitrous oxide has been cited as either having no effect upon respiration or of being a moderate stimulant. Actually, nitrous oxide, like any other anaesthetic, does cause a slight increase in the depth of anaesthesia just as the patient falls asleep. With nitrous oxide, however, the patient never gets much deeper than this stage so that it appears to be a stimulant. If the gas is added to a mixture of other drugs the respiration is either unaffected or very slightly depressed, although hypnosis and analgesia are remarkably reinforced. Trichlorethylene is said not to affect the circulation during light anaesthesia and, although relatively benign cardiac irregularities do occur, the student's mind need not, at this stage, be confused by them. These points, therefore are left to the person using the charts for teaching purposes.

These charts were originally constructed to facilitate instruction during a lecture demonstration tour of Pakistan, India, Ceylon, Burma and Iraq (under the auspices of The British Council) in the winter of 1951–52. They proved invaluable then and afterwards as teaching devices during undergraduate instruction and for the elementary training of resident anaesthetists. Not the least of their uses has been to explain to interested surgeons why anaesthetists have graduated into polypharmacy.

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Printed in Great Britain by JOHN SHERRATT & SON, Park Road, Altrincham